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The American Heart Journal

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The American Heart Journal

VOL. 9 AUGUST, 1934 NO. 6

Original Communications

ACUTE PULMONARY CONGESTION AND CARDIAC ASTHMA IN PATIENTS WITH MITRAL STENOSIS*

SYLVESTER MCGINN, M.D., AND PAUL D. WHITE, M.D.
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ACUTE pulmonary congestion with or without cardiac asthma is most commonly observed with failure of the left ventricle.[1] There is, however, a much smaller group of patients with mitral stenosis who suffer similar attacks, and in such cases the left ventricle is not primarily involved. The clinical records of patients with mitral stenosis and acute pulmonary congestion have been reviewed by us to determine what characteristics differentiate this condition from that more frequently seen due to left ventricular failure.

Cardiac asthma is a term applied to a kind of dyspnea peculiar to organic heart disease. It is paroxysmal in nature, with distressing wheezing respiratory difficulty similar to that seen in bronchial asthma; it may or may not be accompanied by the expectoration of blood-tinged frothy sputum. Sudden failure of the left ventricle which has been weakened by the strain thrust upon it by hypertension, a lesion of the aortic valve, or coronary thrombosis causing myocardial infarction is primarily responsible for the greater number of cases. As the inefficient ventricle fails to expel all of its contents into the general circulation, blood piles up in the pulmonary field and through the mechanism of a reflex nervous action initiates a paroxysm of rapid breathing accompanied by wheezing (asthmatic) respiration. The attacks usually occur at night when the individual is reclining in a horizontal position and are due then most likely to the stasis of blood in the pulmonary vessels as the result of the position and of the diminished output of the weak left ventricle during sleep. Cardiac asthma may or may not be associated with moist râles in the lung bases, depending upon whether or not the failure is of sufficient degree to cause only vascular engorge-

*From the Cardiac Clinic and Laboratory of the Massachusetts General Hospital.

ment or whether it exceeds this point to produce actual edema and hemorrhages into the alveoli. In one of Merklen's[2] lectures published by Heitz in 1908 it is stated that cardiac asthma is due usually to failure of the left ventricle, that in such a condition the lungs are generally clear of evident edema, but that there is a type associated with acute pulmonary edema in which there are moist râles at the lung bases, cough, and expectoration of serous sputum. Riesman[3] in 1907 described acute pulmonary edema occurring at night with or without asthmatic breathing, in cases of arteriosclerotic heart disease.

ACUTE PULMONARY CONGESTION WITH MITRAL STENOSIS

The literature contains very little concerning the group of cases in which there is acute pulmonary congestion, with or without asthmatic breathing, as the result of mitral stenosis.

Vaquez[4] has stated that although pulmonary congestion in mitral stenosis is usually a slow and insidious process, there are acute forms associated with overexertion; he erroneously referred to this pulmonary congestion as failure of the right heart. In discussing pulmonary edema in mitral stenosis, Robinson[5] said, "Paroxysmal attacks resembling asthma are sometimes seen. Cough and expectoration, sometimes bloody or blood-streaked, occur. Hemoptysis is not uncommon." Gallavardin[6] in 1921 presented a number of cases to illustrate three types of acute pulmonary edema: (1) that in which the left ventricle fails as a result of rheumatic myocarditis, (2) that due to chronic mitral and aortic endocarditis, and (3) that in which it is secondary to pure mitral stenosis. In the second group he presented two cases having mitral stenosis and an associated aortic lesion. One was a woman of thirty-three years who had had slight attacks when she overexerted herself and four severe attacks with expectoration of frothy sputum without any known provocative cause. The other was a woman fifty-six years of age who complained of violent attacks of smothering at night, one of which required venesection. In the third group he included four cases. The first was a woman thirty-five years old who had nocturnal smothering immediately on getting into bed, and an hemoptysis once a week sufficient to fill a basin. A woman forty-three years old had severe dyspneic attacks after coitus or unusual effort. Another woman thirty-five years of age had violent smothering attacks with the expectoration of bloody sputum following coitus and twice after a warm tub bath. The fourth case was a woman fifty-two years old who had severe attacks of dyspnea with expectoration of frothy sputum and a whistling in her chest when she walked fast. All these patients had dyspnea on effort; two had no peripheral evidence of cardiovascular failure; and digitalis failed to relieve the symptoms in three.

In 1923 Saloz and Frommel[7] reported the case of a woman thirty-seven years old with pure mitral stenosis. She had fallen while hurry-

ing in the street and was brought into the hospital cyanotic, in a cold sweat, breathing rapidly, and with frothy sputum coming from the mouth. A venesection proved to be very beneficial for the immediate attack, but she died some days later. The post-mortem examination showed a mitral stenosis with a large left auricle and right ventricular hypertrophy.

A case with discussion has recently been presented by Thums,[8] the patient being a twenty-eight-year-old man with mitral stenosis who suffered attacks of rapid breathing, hemoptysis, and precordial pressure following the exertion of skiing and snowshoeing. He improved while on digitalis therapy and abstinence from exercise.

THE PRESENT SERIES

We have reviewed a series of 20 cases of our own showing mitral stenosis associated with acute pulmonary congestion. Of this group, 10 had mitral valve disease alone, whereas the other 10 had a coexisting aortic lesion or hypertension. All of the second group had cardiac asthma, while 5 of the former had definite wheezing, the other 5 having severe paroxysmal attacks of dyspnea with hemoptysis or pink frothy sputum but without a clear history of wheezing. The average ages of the two groups when last heard from was 31.3 and 50 years respectively, half of the patients of the second group being over 50 years of age whereas none of the first group had reached their fiftieth year. These figures should be contrasted with those in a series of 272 cases of cardiac asthma of all etiologies that we have recently reported,[1] 90 per cent of whom, or 246 patients, were over 50 years of age; 96 per cent, or 260 cases, of that series showed no mitral stenosis and so may be compared with interest with the present series of 20 cases with mitral stenosis (Table I).

Eight of our 10 patients having mitral stenosis complicated by hypertension or aortic valve disease have died, after an average duration of life from the first attack of asthma of 1.9 years. The other two patients are in fair health to date, having survived eight years and five years respectively, an average of 6.5 years, which exceeds the expectancy of two years derived from the analysis of the above-mentioned group of 272 cases. Six of the 10 patients in the group of patients with uncomplicated mitral stenosis are living, but their activity must through necessity be greatly limited. Their average duration of life since the first attack of pulmonary edema has been 3.5 years. The average duration of life of the four patients who have died was 3.9 years from their first attacks of pulmonary edema to death. Two of these four patients died during attacks of pulmonary edema, and the other two died after progressive myocardial failure. It is of interest to note that the paroxysmal attacks ceased to recur in 4 of the patients with complicated mitral stenosis,

while each of two of the uncomplicated cases had one attack with hemoptysis and thereafter no more attacks.

Exertion in some form or other was the factor precipitating the attacks of acute pulmonary congestion in 7 of the 10 cases with mitral stenosis plus strain on the left ventricle and in 8 of the cases with pure mitral stenosis. A survey of our general series of cardiac asthma without mitral stenosis indicated that only 23, or 8 per cent, had attacks

TABLE I

ACUTE PULMONARY CONGESTION. A COMPARISON OF CASES WITH AND WITHOUT MITRAL STENOSIS

	MITRAL STENOSIS WITHOUT CAUSE FOR LEFT VENTRICULAR HYPERTROPHY	MITRAL STENOSIS WITH A LESION TO CAUSE LEFT VENTRICULAR HYPERTROPHY	CASES OF A FORMER SERIES WITHOUT MITRAL STENOSIS
Number	10	10	260
Sex Males	6	7	196
Females	4	3	64
Cardiac asthma	5	10	260
Number who have died	4	8	232
Number over 50 years of age	0	5	239
Average age at onset of attacks	26	47	58
Duration since onset of attacks to last report of living patients	3.5	6.5	4.1
Average age at death or last report	31.3	50	59.6
Duration in years from onset of attacks to death	3.9	1.9	1.6
Rheumatic history	7	6	11
Attacks brought on by exertion	8	7	23
Attacks brought on by coitus	3	2	
Attacks brought on by paroxysmal tachycardia	5	1	
Frank hemoptysis	7	1	50
Frothy sputum	7	6	70
Mitral insufficiency	3	8	5
Aortic stenosis and insufficiency	0	4	8
Aortic insufficiency	0	3	48
Hypertension	0	5	167
Angina pectoris	0	4	44
Auricular fibrillation	3	3	29

initiated by exertion, the vast majority occurring while the patient was in bed and at rest during the night; of those 23 patients 3 had rheumatic mitral disease, 5 had luetic aortitis, 4 had arteriosclerotic coronary disease, and 11 had hypertension. In 12 of those patients the attacks were so frequent as to occur either in the day or in the night. The types of exertion most frequently found to produce attacks in our present series of 20 cases were coitus in 5, bathing in 3, and frequently excitement and fast walking. Five of the uncomplicated cases of mitral stenosis had pulmonary congestion with the onset of attacks of paroxysmal tachycardia. We believe that this difference in the factors precipitat-

ing attacks of acute pulmonary congestion in patients with and without mitral stenosis is of special significance.

The clinical histories show that one of our 10 cases with complicated mitral stenosis had frank hemoptysis in contrast to 7 of the 10 uncomplicated cases, while the presence of frothy sputum was noted 6 and 7 times respectively in the two groups. Angina pectoris coexisted with cardiac asthma in 4, and auricular fibrillation in 3, of the cases of our group with mitral stenosis and left ventricular hypertrophy, whereas none of the 10 patients with uncomplicated mitral stenosis had angina pectoris and 3 had auricular fibrillation. A history of having had either rheumatic fever or chorea was noted in the case of 7 of the patients with uncomplicated mitral stenosis and of 6 of the patients with complicated mitral stenosis. In the latter group aortic stenosis and insufficiency occurred together in 4 cases and aortic insufficiency without stenosis of clinical importance in 3; hypertension was present in three. Mitral insufficiency was noted clinically in 8 of the complicated cases and in 3 of the uncomplicated series.

Clinical or roentgenographic studies presented evidence indicating left ventricular hypertrophy in all the cases having hypertension or aortic disease associated with the mitral stenosis. X-ray evidence was available in 8 of the other 10 cases, and all showed "mitral shaped" hearts with enlarged left auricles and prominence in the region of the pulmonary conus. General enlargement of the heart was seen in 4 of these cases, but it was thought to be of right-sided origin, and in no case was left ventricular enlargement noted. Neither of the remaining 2 cases of uncomplicated mitral stenosis showed enlargement of the heart to the left by percussion in the fifth intercostal space. Nine patients in the group with mitral stenosis complicated by another lesion had electrocardiograms taken, three of which showed auricular fibrillation and two showed an abnormal axis deviation, to the left in both instances. Electrocardiograms were also made on 9 of the patients with uncomplicated mitral stenosis, two of which showed auricular fibrillation, one auricular flutter, four large P-waves, and 5 a right axis deviation.

Postmortem Examinations of Cases With Uncomplicated Mitral Stenosis.—Three hearts of the 10 cases of our series with uncomplicated mitral stenosis were examined post-mortem.

The first of the post-mortem examinations was made on a man thirty-two years old, who died six hours after the onset of acute pulmonary congestion. The heart weighed 560 grams. The right ventricular wall thickness varied between 5 and 8 mm. in thickness, while the left ventricular wall was 10 mm. in thickness. The left ventricle was full-sized, the left auricle considerably dilated, and the chambers on the right side were markedly dilated. The mitral valve was noted as being button hole in type with fibrocalcareous changes; the opening measured 1½ cm. by 5 mm. The aortic valve was normal. Edema of the lungs was present, the pulmonary tissue being described as of spongy consistency and salmon colored in appearance. The liver was small.

The second case was that of a thirty-five-year-old woman who died with acute pulmonary edema. The heart weight was 325 grams; the right ventricular wall measured 10 mm. in thickness, and the left ventricular wall measured only 11 mm. The mitral valve was markedly stenosed, measuring only 3.3 cm. in circumference; it was not calcified. The aortic valve was negative. Pulmonary congestion was present in the lungs, which had large acrepitant areas.

The third case was that of a twenty-eight-year-old man who died after six weeks of progressive failure. The heart weight was 528 grams, and the right and left ventricular walls measured 6 mm. and 10 mm. respectively. There was slight dilatation of the left ventricle and considerable enlargement of the left auricle and of the chambers on the right side of the heart. The mitral valve consisted of a fibrocalcareous mass surrounding a crevicelike slit. The aortic valve was normal. The lungs were voluminous, of a leathery consistency, and yielded a moderate amount of frothy fluid. One pulmonary infarct was noted. The liver was of firm consistency and had a nutmeg appearance.

DISCUSSION

Gallavardin[6] believed that acute pulmonary edema took place as a consequence of the failure of the left auricle in cases of uncomplicated mitral stenosis. He observed that these attacks occurred only when there was a normal rhythm of the auricles and when they were not tremendously enlarged. In our cases which correspond to his, one had auricular flutter, 3 had auricular fibrillation, and 5 had attacks of acute pulmonary congestion with paroxysmal auricular tachycardia or fibrillation. X-ray films showed left auricular enlargement in all of our 8 patients with uncomplicated mitral stenosis who had roentgenograms made.

The theory of Saloz and Frommel[7] with regard to acute pulmonary edema consequent to mitral stenosis is that there is a failure of the left ventricle. Their conception of the mechanism was based upon the experimental work of Henderson and Prince,[9] who demonstrated the closely controlled relationship between the right and left ventricles. The work consisted of measuring the systolic outputs under various pressures in the cat's heart, and the inference drawn was that the greater the pressure in the pulmonary circuit the greater would be the systolic output of the left ventricle; hence great pulmonary congestion would be inhibited. It was also shown that when the pressure in the pulmonary vessels was low, the output of blood per beat of the left ventricle would be diminished and thus desanguination of the lungs would be avoided.

One factor is present, however, in the problem under discussion to which Saloz and Frommel[7] failed to give full consideration, and that is the effect of mitral stenosis on the normal flow of blood. Henderson and Prince[9] observed that the pressures described in their work on the hearts of normal cats were not invariable and depended to a great degree on the tonus of the heart and the integrity of the valves. The hypertrophy and dilatation of the left auricle and of the right chambers in mitral stenosis are strong evidence that this lesion (mitral stenosis) disturbs the equilibrium existing between the greater and lesser cir-

culations and tends to prevent the left ventricle which may be of normal size and tonus from fulfilling its usual performance of work and sending out a normal amount of blood.

There are certain features that distinguish acute pulmonary congestion when mitral stenosis is present from that in which there are hypertrophy, dilatation, and failure of the left ventricle. The burden of the strain imposed by the stenosis of the mitral valve is borne by the left auricle, the pulmonary vessels, and the right heart. As might be expected, the incidence of a rheumatic infection is high in those cases with mitral stenosis, occurring in 13 of our 20 cases, which figure compares with that of only 11 patients thought to have had rheumatic heart disease in our previously reported series of 260 cases of cardiac asthma without mitral stenosis.

Acute pulmonary edema with uncomplicated mitral stenosis appears at an earlier age, and the prognosis is better for duration of life than in the cases with left ventricular enlargement and failure. Frank hemoptysis also is more common in cases of uncomplicated mitral stenosis. Exertion or paroxysmal tachycardia is the precipitating factor of the pulmonary congestion in nearly every case of uncomplicated mitral stenosis; without tachycardia the patient is free from attacks. It is a striking fact that digitalis fails to be as beneficial in this group in which there is mechanical difficulty as it is in those cases with left ventricular strain and failure.

Oppenheimer and Schwartz[10] have recently reported 3 cases having paroxysmal pulmonary hemorrhages, the patients being young individuals with mitral stenosis and without any known cause for left-sided hypertrophy. A post-mortem examination was made on one of the cases. Palpitation was a common symptom preceding the dyspneic spells, two of which were accompanied by asthmatic breathing, and pulse rates of 170, 160, and 140 were noted during attacks in the three patients. Electrocardiograms on one patient were reported as invariably showing a normal sinus rhythm.

Our conception as to the mechanism producing acute pulmonary congestion differs from those given above. We believe that when the heart is speeded up by effort, excitement, or paroxysmal tachycardia, the strong enlarged right ventricle of these hearts with mitral stenosis but without heart failure expels more blood into the pulmonary circulation than can be passed through the stenosed mitral valve in the same unit of time. Cardiac asthma may or may not appear at this time; the process may proceed to excessive formation of edema giving moist râles, to frank hemoptysis, and even to death. This theory is in accord with the ideas of Wenckebach, Shellong, and Thums, who have considered the importance of the hyperactivity of the right ventricle in such cases. Failure of the right ventricle may occur secondarily, with a consequent tricuspid insufficiency and a backing up of

the blood peripherally into the neck veins and into the liver, with relief of the intense pulmonary congestion. An alternative, less plausible, explanation of acute pulmonary congestion with mitral stenosis is that the left ventricle in such cases, small or of normal size and unaccustomed to expel much blood because of its underfilling resulting from the obstruction due to the marked mitral stenosis, fails abruptly when it is suddenly supplied with an increased volume of blood, the surplus remaining behind to cause the pulmonary congestion. If, however, the mitral stenosis is of sufficient degree in these cases to prevent an adequate amount of blood from entering the left ventricle at ordinary heart rates, it is extremely unlikely that this same obstruction will fail to protect the left ventricle from any gross oversupply of blood when the heart is beating rapidly. The left ventricle in such cases should, like the left ventricle in the normal heart, be able to deal with the increase in blood supplied to it at increased heart rates, since the left ventricle itself is not diseased (as indicated by the postmortem examinations of the three cases referred to above) and since the extra volume of blood will not be as great as that which would result from tachycardia in a heart without the obstruction of mitral stenosis. The normal left ventricle does not fail when it is temporarily given more blood during tachycardia.

In cases of mitral stenosis associated with an enlarged and dilated left ventricle due to systemic hypertension or to an aortic valve lesion, we may assume that either or both of the above described mechanisms causing acute pulmonary vascular congestion may be effective. A patient having such lesions may have attacks of acute pulmonary congestion with hemoptysis following exertion at an early stage and later have similar attacks with frothy sputum rather than hemoptysis coming on while at rest, especially in sleep (we have noted three such cases).

SUMMARY

We have made a study of 20 cases of mitral stenosis with attacks of acute pulmonary congestion with or without cardiac asthma; 10 were uncomplicated and 10 were complicated by factors (aortic valve disease or hypertension) causing strain on the left ventricle. We have compared the findings in these groups with those in a group of much more common cases, namely, those of acute pulmonary vascular congestion with cardiac asthma without mitral stenosis. Three of the 10 cases with uncomplicated mitral stenosis were examined after death.

In the large group of cases with left ventricular strain and failure, acute pulmonary congestion is found in older persons, comes on most often while the patient is at rest, has a poor prognosis, but may be successfully treated for a while with digitalis and diuretics. Here the

acute pulmonary congestion evidently results from a backing up of blood in the pulmonary vessels due to the inability of the left ventricle to expel its full contents.

In the small group of cases of uncomplicated mitral stenosis, acute pulmonary congestion is observed in younger patients; the attacks are precipitated by exertion or paroxysmal tachycardia and are often accompanied by frank hemoptysis; the prognosis is more favorable than in most other cases of cardiac asthma, although digitalis and diuretics are of less value. Here the best explanation of the acute pulmonary congestion is that when the heart is stimulated to greater work, the hypertrophied and dilated right ventricle propels more blood into the pulmonary vessels than can pass through the stenosed mitral valve in the same unit of time, with a consequent acute pulmonary congestion.

The case reports upon which this study is based will be published with the reprints of this article. Reprints may be obtained from the authors on request.

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HUGE T-WAVES IN PRECORDIAL LEADS IN CARDIAC INFARCTION*

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THE electrocardiographic study of acute coronary occlusion with chest leads is bringing to light certain new features. One of the phenomena which has interested us recently is the occurrence of huge T-waves in precordial leads in this disease.[1, 2] The present paper is a report of seven cases showing this finding.

Six of the seven cases showed huge upright T-waves in Leads IV or V,† which exceeded 13 mm. in amplitude. One case showed a very large inverted T-wave in Lead V, 19 mm. deep. The electrocardiographic string deflection was standardized carefully in each instance, and skin resistance was kept low, so that no "overshooting" occurred. Therefore we feel confident that this electrocardiographic phenomenon cannot be attributed to an artefact.

The occurrence of large T-waves in limb leads in coronary occlusion has been noted by several observers, among others Levine and Brown,[3] Katz and Bohning,[4] and Cooksey.[5] In some cases these waves have a quite distinctive appearance. In others, they look like large normal T-waves.

The huge inverted T-waves which appear in Lead V of Case 7 do not differ greatly from those seen in certain patients without coronary occlusion. We have seen a T-wave in Lead V, 13 mm. deep in a presumably normal college student.[6] However, when these huge waves are upright in direction (Cases 1 to 6) they present an appearance which differs distinctly from anything we have seen in a series of 550 controls.‡ We therefore consider the huge upright T-wave in Lead IV or V an important diagnostic feature of acute or subacute cardiac infarction.

Fairly large upright T-waves often appear in precordial leads during the healing of an anterior cardiac infarct.[1] However, among a group of 78 patients with acute coronary occlusion, which has been studied with chest leads,[7] these 6 are the only cases in which the T-wave in Lead IV or V has exceeded 10 mm. in height.

*From the Edward B. Robinette Foundation, Medical Division, Hospital of the University of Pennsylvania.

†The various chest leads are designated by the numbers IV, V and VI as in a previous communication.[1]

‡The controls consist of 200 patients with various types of cardiovascular disease, and 350 patients in whom no evidence of heart disease could be elicited. Two hundred and fifty of the latter are college students.[6]

CASE REPORTS

CASE 1.—W. S., a man of fifty-seven years, was well until Sept. 28, 1932. That morning at 9 A.M., as he was walking out of his front door preparing to go to work, he was seized with a "terrible" pain across the left side of the chest in the region of the nipple. He went to bed, took some hot water, and in fifteen minutes the pain began to abate. As he started downstairs once more, he experienced another similar attack. He lay down and took some more hot water. In twenty minutes this attack subsided, but a soreness persisted in his chest for an hour longe.. He then went to work on his butter and egg route. At 3:30 P.M. the pain began again. He went home and after an hour this third attack wore

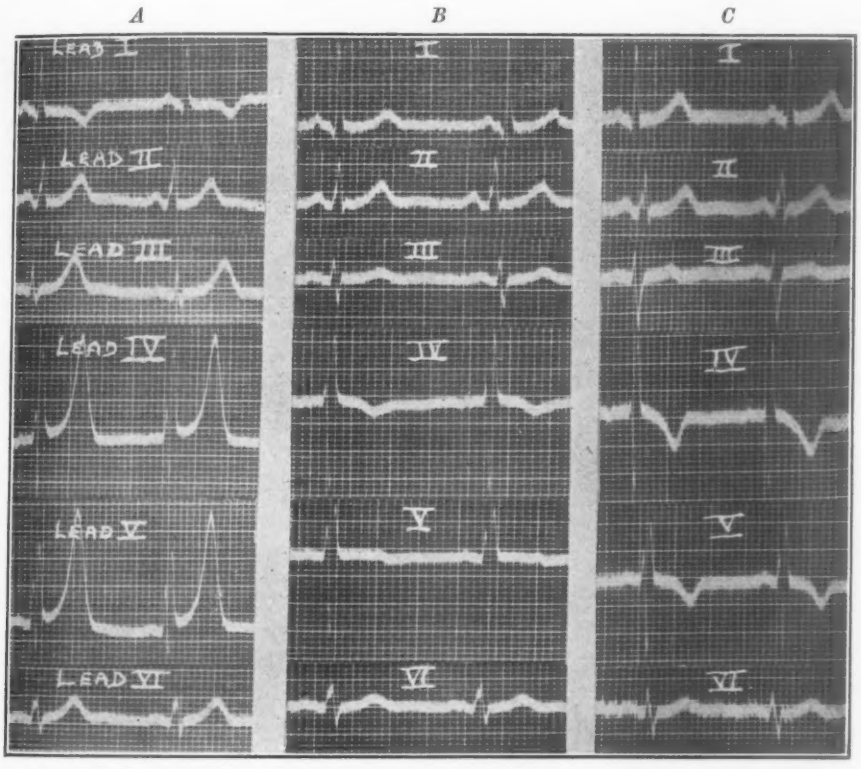

Fig. 1.—Electrocardiograms of Case 1. The various chest leads are designated by numbers IV, V, and VI as in a previous communication.[1] The anterior electrode in Leads IV and V was placed in the fourth left interspace, 4 cm. from the sternum.

A, Tracing taken on Nov. 3, 1932, five weeks after the onset. T_1 is inverted, T_2 and T_3 are quite large. T_4 is +18 mm. T_5 is +22 mm. The QRS complex in Leads IV and V is M-shaped, resulting from small upward deflection, preceding the initial downward deflection. The RS-T interval is slightly elevated in Leads IV and V. No other chest leads were taken on this date.

B, Tracing taken on April 17, 1933, seven and a half months after the onset. The QRS complexes are somewhat similar to those of Nov. 3. The T-waves have changed markedly. The huge T-waves in Leads IV and V have disappeared and T_1 has become upright. Moving the anterior chest electrode to a point over the apex-impulse caused a slight reduction in size of the initial upward deflection of QRS in Leads IV and V, but did not change the T-waves.

C, Tracing taken on Dec. 28, 1933. Definite changes are evident. The only abnormalities remaining in the electrocardiogram are a left axis deviation, slight slurring of QRS, especially in Lead II, and an initial upward deflection of QRS in Lead V, 4 mm. high. Moving the anterior chest electrode to the apex and beyond caused the initial upward deflection of QRS_5 to disappear, but did not alter the T-waves.

off. The next day he went to work and has continued his occupation since that time. He says, however, that he felt "washed out" for two months. After December, 1932, he felt well, except for attacks of intermittent claudication induced by walking seven or eight blocks. These attacks are more marked in the right leg. He was last seen on Dec. 28, 1933. He had experienced a few mild anginal attacks induced by effort, during the preceding month.

This patient first came to the cardiac clinic of the Hospital of the University of Pennsylvania on Oct. 31, 1932, about five weeks after the onset. He was a well-nourished male. The blood pressure was 160 mm. systolic and 95 mm. diastolic. The heart was normal in size and shape (orthodiagram). There were no signs of congestive failure. Auscultation revealed a harsh systolic murmur at the apex, a softer systolic murmur at the base, and an accentuated second sound. The sounds were slightly distant. The blood count and urine analysis showed normal findings (WBC were 7,300). The blood Wassermann reaction was negative. During his last visit on Dec. 28, 1933, the blood pressure was 120 mm. systolic and 85 mm. diastolic. The heart sounds were normal except for a rather rasping reduplication of the first sound at the apex. No other changes were noted in the general physical examination or orthodiagram.

Electrocardiograms (Fig. 1) were taken on Nov. 3, 1932, April 17, 1933, Dec. 28, 1933. The first tracing, five weeks after the onset, showed an inverted T-wave in Lead I and huge T-waves in Leads IV and V. The second tracing showed a disappearance of the huge T-waves and certain other changes in the ventricular complexes. The last tracing showed a normal electrocardiogram except for slurring of the QRS complex in Lead II, left axis deviation, and an upward deflection preceding the downward deflection of QRS in Lead V.

Summary: A fifty-seven-year-old man suffered three severe attacks of precordial pain on Sept. 28, 1932. On Nov. 11 while the patient was still feeling below par, the electrocardiogram showed huge T-waves in Leads IV and V. These large waves disappeared subsequently. The electrocardiogram a year later showed normal T-waves and a few slight abnormalities of QRS.

CASE 2.—W. M. B., whose case has been reported,* was a man of fifty-four years, who had attacks of pain over the heart on Oct. 12 and on Dec. 22, 1932. He died Dec. 30, 1932, in a third severe attack which began on Dec. 28. Necropsy showed an infarct in the anterior surface of the left ventricle. The electrocardiogram on Dec. 24 showed huge T-waves in Leads IV and V, 15 mm. high.

CASE 3.—M. G. was a man of fifty years of age. Since 1929 he had experienced attacks of dull pain in the ulnar side of the left forearm radiating up to the shoulder and to the precordium. The attacks were induced by effort, emotion and the ingestion of food. They were relieved by rest and relaxation. On Feb. 17, 1933, at 7 A.M., shortly after arising from bed, he was seized with a severe agonizing pain in the left forearm, which rapidly extended up the arm and into the precordium. It was partly relieved by morphine after thirty minutes, but it returned and persisted as a rather severe dull ache for twenty-four hours. He was admitted to the Hospital of the University of Pennsylvania, on the service of Dr. Alfred Stengel on Feb. 17. The blood pressure was 120 mm. systolic and 80 mm. diastolic. The heart sounds were distant; the left border of the heart was 10 cm. from the midsternal line; there were no signs of congestive failure. The next day, fever (102° F.) and leucocytosis (12,300) appeared. Slight fever

*See Reference 1, Case 19, Chart 4.

persisted for ten days. The leucocyte count reached 20,000 on Feb. 19 and subsided to normal on Feb. 27. The blood pressure dropped to 100 mm. systolic and 70 mm. diastolic on Feb. 19, and a few râles appeared at the right base. He gradually improved and was discharged on April 8. During his stay in the hospital he suffered frequent attacks of moderately severe aching pain in the region of the left elbow, every day or two, for six weeks. The most severe attack occurred on March 16 and lasted several hours. No pain was felt in the precordium after the first twenty-four hours of hospitalization. On Feb. 18 urinary retention necessitated catheterization. This was followed by a relatively mild urinary tract in-

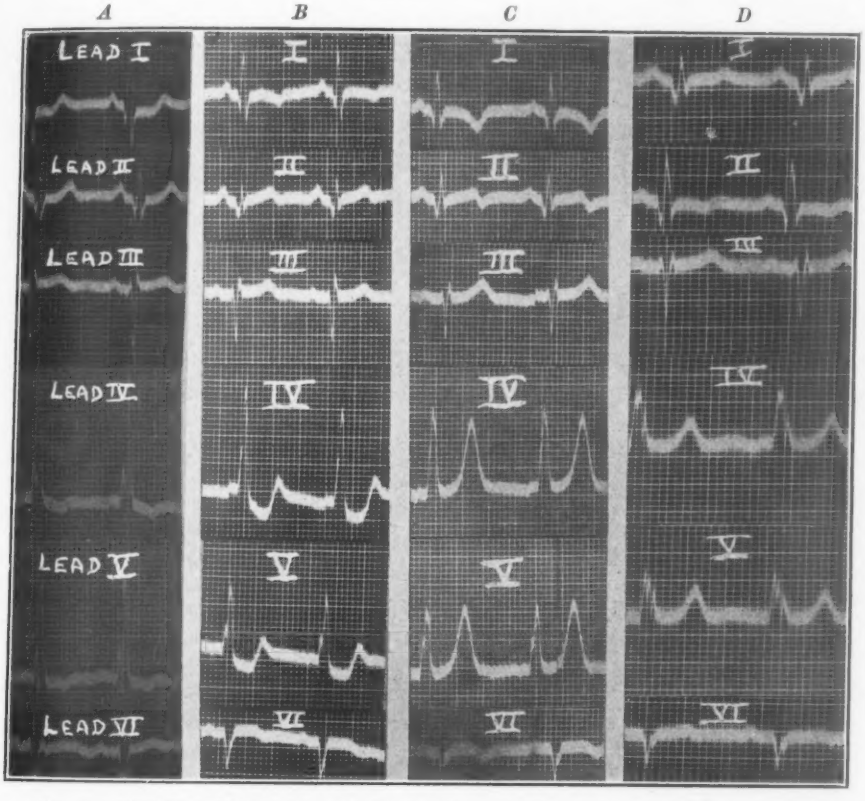

Fig. 2.—Electrocardiograms of Case 3. The patient had an attack of probable coronary occlusion on Feb. 17, 1933, beginning at 7 A.M. The chest leads in this figure were taken with the anterior electrode at the apex impulse, and the posterior electrode in the usual position at the angle of the left scapula.

A, Tracing taken on Feb. 17 at 5 P.M. The RS-T interval is slightly depressed in Lead I. QRS_4 and QRS_5 are somewhat M-shaped. No RS-T interval deviations could be elicited in the chest leads, although the anterior electrode was moved to various positions on the precordium and beyond the apex impulse.

B, Tracing taken on Feb. 20. The typical signs of an acute anterior infarction are present. T_1 is inverted. The initial downward deflection of QRS in Leads IV and V is absent. The RS-T interval in Leads IV and V is depressed below the isoelectric line. The T-wave in these leads is beginning to turn upward. No other chest leads were taken.

C, Tracing taken on March 28. T_1 is deeply inverted. The initial downward deflection of QRS in Leads IV and V is absent. T_4 is +14 mm. T_5 is +12 mm. No other chest leads were taken.

D, Tracing taken on Jan. 6, 1934. The signs of an old anterior infarct are still present. Other tracings taken with the anterior electrode on the fourth left rib, 4 cm. from the sternum showed an M-shaped QRS complex, but no difference in T-waves. (The tracing labelled "Lead I" is Lead II, and vice versa.)

fection. On March 23 he suffered a right brachial embolus, the symptoms of which were not particularly disturbing.

After discharge on April 8 he lived a fairly restricted life and felt quite comfortable. When last seen Jan. 6, 1934, he was working as a tailor. His attacks of effort angina had become more frequent, and more readily induced since November, 1933. The blood pressure was 140 mm. systolic and 80 mm. diastolic. There was moderate enlargement of the heart (orthodiagram). There were no signs of congestive failure, and no significant murmurs; the heart sounds were distant.

Repeated electrocardiograms were taken (Fig. 2). The first, on the day of onset (Feb. 17, 1933) showed no very definite RS-T interval deviations. The main abnormality was an absence of the initial downward deflection of QRS in Lead IV; the T-waves were upright in the limb leads and not large. On Feb. 20, T_1 was inverted (–1 mm.); and Lead IV showed the signs of recent infarction in the anterior surface of the left ventricle.[1] On Feb. 28, T_1 was more deeply inverted (–3 mm.) and T_4 was 6 mm. high. On March 6, T_1 was still –3 mm. and T_4 was +10 mm. On March 16, T_1 was –4 mm. and T_4 was + 14 mm. On March 28, T_1 was –3 mm., T_4 was +14 mm. On Jan. 6, 1934, the signs of an old infarct in the anterior surface of the left ventricle were still present; T_4 was +4 mm. and Q_4 was absent. From results which we have obtained in subsequent patients, we are inclined to believe that a much larger upright T-wave in Lead IV might have been obtained on Feb. 28 and thereafter, by varying the position of the anterior chest electrode. (See Fig. 6.)

It is not entirely clear in this case, how much of the fever and leucocytosis was due to the urinary tract infection. Nevertheless, there is little doubt that the patient suffered a coronary occlusion, possibly a slowly developing occlusion, beginning on the morning of Feb. 17, 1933.

Summary: A fifty-year-old man, who had previously suffered from effort angina, developed the symptoms and signs of a coronary occlusion on Feb. 17, 1933. Huge upright T-waves appeared in Lead IV, several weeks after the onset, and disappeared subsequently.

CASE 4.—S. B., a woman of sixty-five years, had been known to have a blood pressure exceeding 200 mm. systolic and 100 mm. diastolic for at least seven months prior to her present illness. She had suffered a few mild anginal pains during this seven months' period. On March 11, 1933, she was admitted to the Hospital of the University of Pennsylvania, on the service of Dr. Alfred Stengel. That morning, without warning, the patient had suffered a severe attack of pain over the heart and in the left hypochondrium, referred to the left shoulder and arm. Both arms felt numb. Extreme weakness, trembling and profuse perspiration occurred, and the patient felt very cold and faint. On admission, the blood pressure was 140 mm. systolic and 70 mm. diastolic. The heart sounds were distant, gallop rhythm was heard at the apex, and occasional extrasystoles were noted. There was slight dyspnea, some pallor, and moist coldness of the skin. The lips were slightly cyanosed. Râles were noted at the lung bases. The acute pain persisted for eight hours; a residual soreness remained for twenty-four hours. During the first six weeks of her stay in the hospital she suffered repeated attacks of dull pain over the heart and in the left hypochondrium. Fever (100° F.) was present on March 12, and disappeared the next day. Recurrent elevations of temperature appeared between April 5 and 16. She remained afebrile after that time. The only elevated leucocyte count was 11,400 on March 12. The lowest blood pressure recorded was 90 mm. systolic and 60 mm. diastolic on the afternoon of her admission, March 11. It then rose to 110 mm. systolic and 70 mm. diastolic and remained

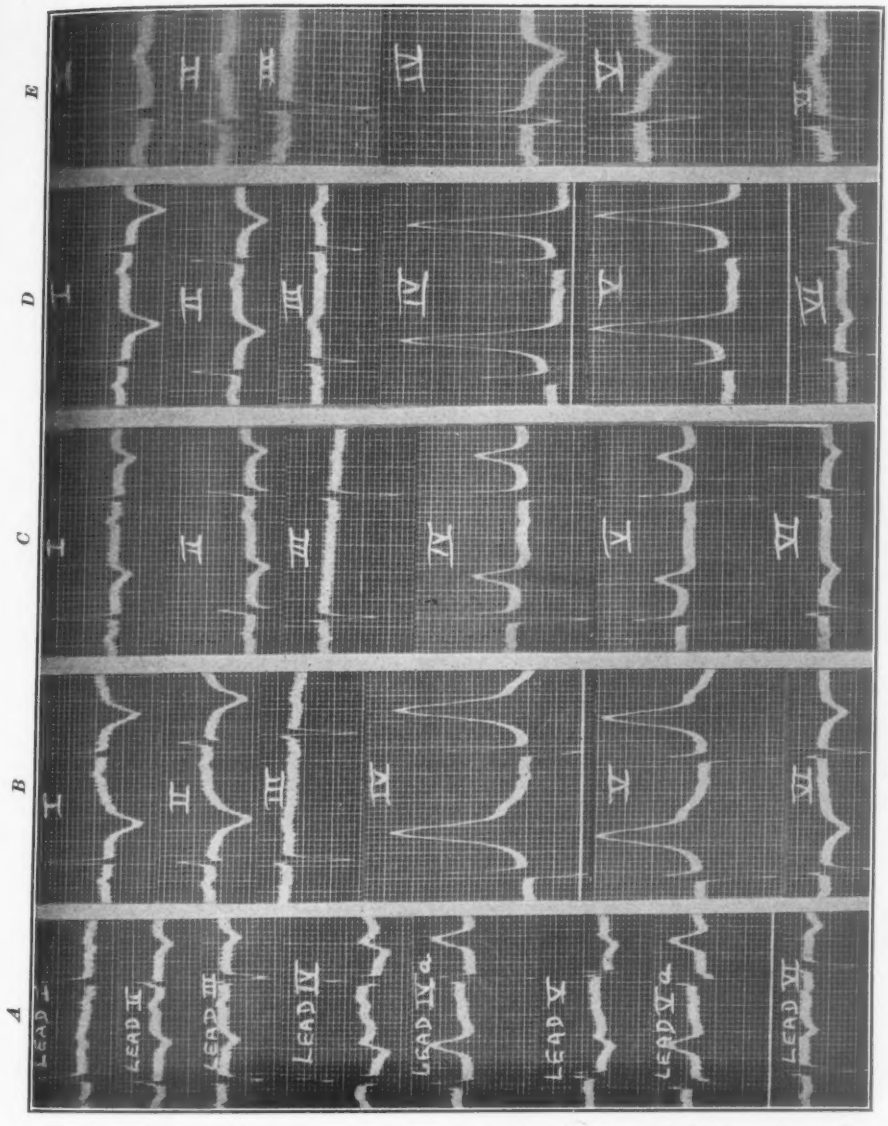

Fig. 3.—Electrocardiograms of Case 4. The patient had an attack of cardiac pain on March 11, 1933. All the tracings in this figure, except when otherwise stated, were taken with the anterior chest electrode at the apex impulse. The largest T-waves were obtained from a point 3 cm. to the left of the apex.

A, Tracing taken March 11. Lead I shows a slight RS-T interval elevation. Lead II shows an inverted T-wave. Lead IV shows a small initial downward deflection of QRS, a slight depression of the RS-T interval, and a diphasic T-wave. Lead V shows an M-shaped QRS complex. Leads IV *a* and V *a* were taken with the anterior electrode 4 cm. to the left of the apex impulse. They show marked differences from Leads IV and V, which were taken from the apex.

B, Tracing taken March 13. Large inverted T-waves have appeared in Leads I and II. Huge upright T-waves are present in Leads IV and V, 24 mm. and 18 mm. high. T_6 has become quite deeply inverted. The RS-T interval in Leads IV and V is slightly elevated.

C, Tracing taken March 20. All the T-waves are smaller.

D, Tracing taken April 10. All the T-waves have become large once more, resembling those on March 13. By May 16 the T-wave had again become quite small.

E, Tracing taken Jan. 6, 1934. Left axis deviation is the only abnormality which has persisted.

below 160 mm. systolic throughout her hospital stay. She was last seen on Jan. 6, 1934. The blood pressure at that time was 220 mm. systolic and 80 mm. diastolic. She was still experiencing mild anginal pain from time to time but was quite comfortable on a limited schedule of activity.

Many electrocardiograms were taken (Fig. 3) March 11, 12, 13, 15, 20, 28, April 10, 20, May 4, 16, 1933, and Jan. 6, 1934. On the first day the tracings varied considerably, depending upon the position of the anterior electrode on the chest, but the T-waves were not especially large. Slight RS-T interval deviations appeared in Leads IV and V. On March 12, the tracing had changed markedly. Huge upright T-waves had appeared in Lead IV, 18 mm. high, which were largest with the anterior electrode placed just to the left of the apex. On March 13, T_4 reached 24 mm. in height. On March 20, it was smaller; on March 28, again somewhat larger. On April 10, it was again huge (25 mm. high). It then gradually became smaller until on May 16, just before discharge, it was no more than 5 mm. in height. The final tracing, taken on Jan. 6, 1934, was practically normal in all leads except for left axis deviation.

Summary: A woman of sixty-five years experienced severe pain over the heart on March 11, 1933. Huge T-waves appeared in Lead IV on March 12 and persisted more or less for five weeks. The tracing at present, Jan. 6, 1934, is normal except for left axis deviation.

Case 5.—Mrs. R. B. was a mildly diabetic woman of sixty-three years, who was admitted to the Hospital of the University of Pennsylvania, on the service of Dr. Alfred Stengel on July 26, 1933. She was thought to be suffering from cholelithiasis on account of severe epigastric pain radiating to the back, and on account of the finding of a large gall stone by x-ray examination, "probably impacted in the cystic duct." However when an electrocardiogram was taken on July 29, a review of her history elicited the following facts: Since the first of June, 1933, she had suffered attacks of pain in the left side of the epigastrium, radiating to the region of the fourth dorsal vertebra. These attacks were induced by effort, and relieved by rest. On July 15 she had a severe attack of pain in the same regions, not induced by effort, lasting two hours. On July 24 another prolonged seizure took place. On July 27 the third attack occurred, while she was in the hospital. It lasted three hours and required morphine (gr. ½) for relief.

On admission, July 26, the blood pressure was 190 mm. systolic and 90 mm. diastolic. There was moderate cardiac enlargement (orthodiagram). No murmurs were heard. No signs of congestive failure were observed. On July 27 cyanosis of the lips and extrasystoles were noted. Slight fever appeared (100° F.) and persisted for three days. On July 29 the blood pressure was 90 mm. systolic and 60 mm. diastolic, and a few basal râles were heard. The leucocytes were not counted during the febrile period. Before and after this period they were within normal limits. The blood pressure varied between 120 mm. and 160 mm. systolic and 80 mm. to 90 mm. diastolic for the next week; then it became stabilized more or less in the vicinity of 160 mm. systolic and 80 mm. diastolic. The patient was discharged Aug. 28 to return to her home for further convalescence. During September she had another attack of probable coronary occlusion. On Oct. 20 she died at home in an attack, more severe and more prolonged than any previous seizure. Permission for necropsy was not obtained.

Electrocardiograms were taken on July 29, 31, Aug. 7, 16, 28 (Fig. 4). On July 29 Lead IV showed a T-wave 15 mm. high. By July 31 the T-waves in the limb leads had become much smaller, and T_4 was only 6 mm. high. Large T-waves in Lead IV were not seen in any subsequent tracing.

Summary: A mildly diabetic woman of sixty-three years suffered severe attacks of pain in the left hypochondrium on July 15, 24, and 27, 1933. The electrocardiogram changed rapidly from day to day, after it was first taken on July 29. Huge T-waves were present in Lead IV on July 29 and disappeared shortly afterward. The patient died Oct. 20, 1933, presumably of coronary occlusion.

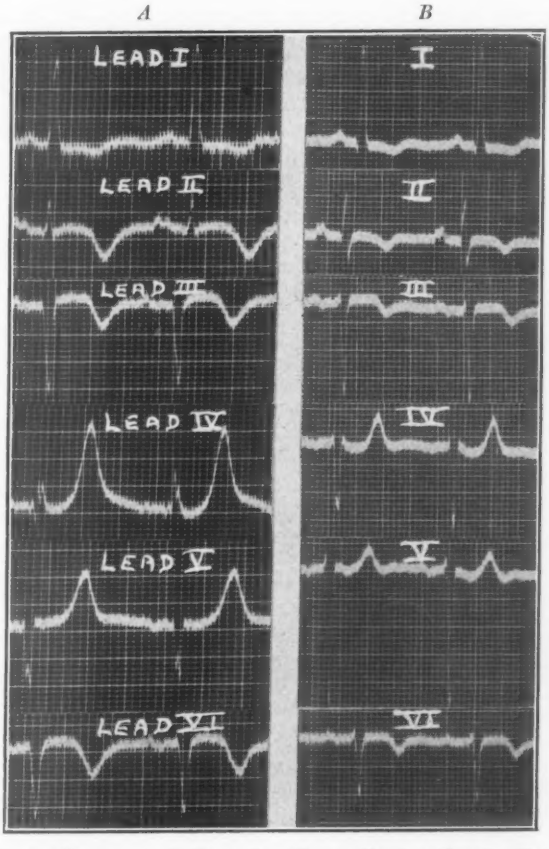

Fig. 4.—Electrocardiograms of Case 5. The patient suffered attacks of cardiac pain on July 15, 24, and 27, 1933. All chest leads were taken with the anterior electrode at the apex impulse. No other chest leads were taken in this case.

A, Tracing on July 29, two days after the last attack of pain. T_1 is diphasic. T_2 and T_3 are deeply inverted. T_4 is +15 mm. T_5 is +9 mm. T_6 is deeply inverted. The QRS complexes in Leads IV and V are quite different. The RS-T interval is practically on the isoelectric line.

B, Tracing taken July 31. The large T-waves in all leads have disappeared. QRS_4 has changed its direction. T_4 and T_5 are still upright but much smaller.

Case 6.—M. W. was a man of fifty-six years. He began to have attacks of severe pain in the lower sternal region on Nov. 1, 1933. The seizures were usually related to eating. They began as a drawing sensation which soon developed into a severe viselike constriction, lasting as a rule about thirty minutes. He had six such attacks during November. He was hospitalized at the Mount Sinai Hospital on Nov. 27, but signed his release on Dec. 10 because he felt well and had experienced only two mild attacks during his two weeks' stay in the hospital. On Dec. 12, he had the most severe seizure of all, during which he coughed up some blood-streaked sputum. Three doses of morphine (amount unknown) were required

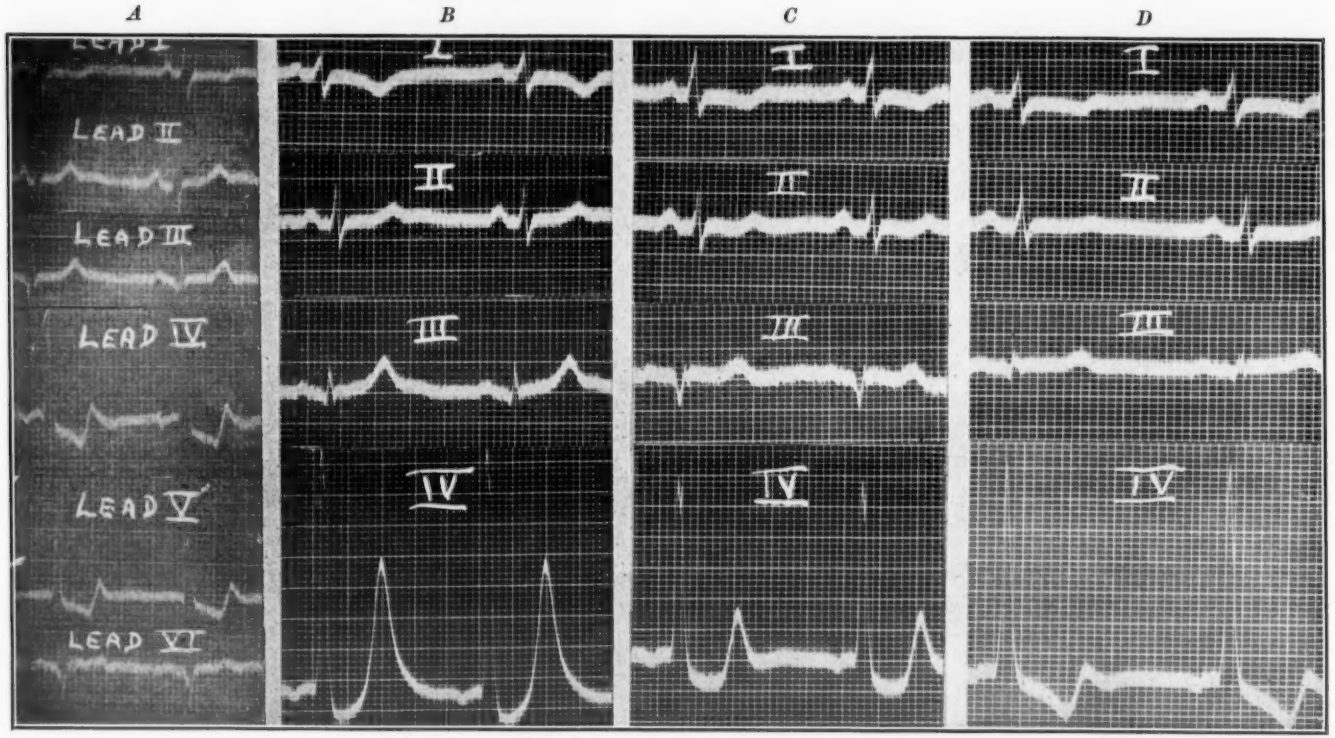

Fig. 5.—Electrocardiograms of Case 6. This patient suffered repeated attacks of cardiac pain. The most severe seizure occurred on Dec. 12, 1933. The tracings shown in this figure were taken with the anterior chest electrode on the fourth rib, 4 cm. to the left of the sternum. The deflections were much larger from this point than from any other on the precordium. (See Fig. 6.) Lead V in this patient was practically identical with Lead IV in B, C and D; consequently it has been omitted from this figure.

A, Tracing taken Dec. 6, given to us by Dr. Joseph Edeiken. T_1 is slightly inverted. T_2 and T_3 are normal. The initial downward deflection in Leads IV and V is absent. T_4 and T_5 are diphasic. There is a slight depression of the RS-T interval, especially in Lead IV.

B, Tracing taken Dec. 12. T_1 is definitely inverted. T_2 is quite large. Lead IV shows a huge T-wave, 20 mm. high. The initial downward deflection of QRS is absent. The RS-T interval is depressed below the isoelectric line.

C, Tracing taken Dec. 15. T_1 is diphasic. T_2 has become smaller. The T-wave in Lead IV has become much smaller.

D, Tracing taken Jan. 22. The limb leads have not changed very much since Dec. 15. T_4 is diphasic.

to relieve the pain. He was admitted to the hospital of the University of Pennsylvania, on the service of Dr. Alfred Stengel on the day of this last attack. The only other noteworthy features of his past history were the use of alcohol daily (8 oz.) for some years, and attacks of intermittent claudication in the left leg since 1925.

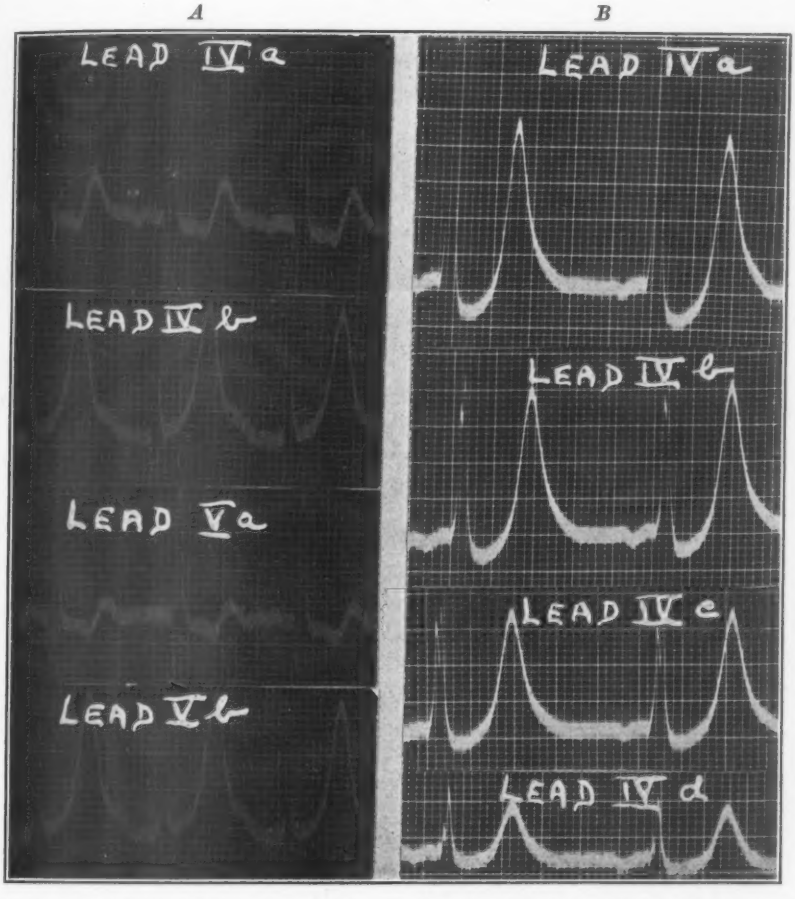

Fig. 6.—Electrocardiograms of Cases 4 and 6, showing the marked differences produced in the chest lead tracings by varying the position of the anterior chest electrode.

A, Electrocardiograms of Case 4, taken March 12. IV *a* is Lead IV with the anterior chest electrode on the fourth rib 4 cm. to the left of the sternum. IV *b* is Lead IV with the anterior electrode 3 cm. to the left of the apex impulse. V *a* and V *b* are Lead V taken with the anterior electrode in the same positions as in taking IV *a* and IV *b*. Marked differences were produced, both in the QRS complexes and the T-waves, by moving the position of the anterior electrode. In this case the "huge" T-waves were obtained from a point 3 cm. to the left of the apex impulse. They were not seen when the anterior electrode was placed on the fourth rib, 4 cm. to the left of the sternum.

B, Electrocardiograms of Case 6 taken Dec. 12. All the tracings were taken with Lead IV, the anteroposterior chest lead. Since Lead V was almost identical, it has been omitted from this figure. *a*, Anterior electrode on the fourth rib, 4 cm. to the left of the sternum; *b*, anterior electrode at the apex impulse; *c*, anterior electrode 4 cm. above the apex impulse; *d*, anterior electrode 4 cm. to the left of the apex impulse.

Case 6 differs from Case 4 in that the T-waves were the largest when the anterior electrode was placed over the fourth rib, 4 cm. to the left of the sternum. They were the smallest when the anterior electrode was placed 4 cm. to the left of the apex impulse.

On admission the patient showed slight cyanosis of the lips. The temperature, pulse, and respirations were normal. There was a difference of blood pressure in the two arms, the right being 74 mm. systolic and 62 mm. diastolic, and the left 142 mm. systolic and 68 mm. diastolic. No pulses could be felt in the arteries of the feet. The lower extremities were cold. The heart sounds were not particularly abnormal. There was no demonstrable enlargement of the heart. A few râles were heard at the left base. A tentative diagnosis of coronary occlusion and Buerger's disease was made.

On Dec. 15, 1933, the temperature reached 99° F. on two occasions. On Dec. 23 it reached 100° F. At other times it has been normal. The leucocyte count reached 12,000 on Dec. 18, 1933, on Jan. 2 and 15, 1934. At other times it has varied from 7,000 to 10,000. Despite continued rest in bed the patient suffered repeated attacks of severe substernal pain every two or three days from the time of admission until Jan. 17. On that day he had a seizure lasting three hours. Since then he has been free from pain. These attacks have been associated with an elevation of the blood pressure from its usual level of 130 mm. systolic and 70 mm. diastolic, to 170 mm. to 180 mm. systolic and 90 mm. to 110 mm. diastolic. Electrocardiographic changes were noted during the last paroxysm, which disappeared after the pain had subsided. Morphine was usually necessary during the attacks. Nitroglycerin gave no relief.

The electrocardiograms are shown in Fig. 5. The first tracing, obtained from Dr. Joseph Edeiken, taken on Dec. 6, showed evidence suggesting a healing infarct in the anterior surface of the left ventricle. The second tracing (Dec. 12) showed huge T-waves in Lead IV, 20 mm. high. By Dec. 15 the huge T-waves had disappeared and certain changes had occurred in the limb leads. Tracings on Dec. 18, and 21, 1933, and Jan. 17, 22, and 26, 1934, have not shown huge T-waves.

Summary: A man of fifty-six years with probable thromboangiitis obliterans suffered recurring pains over the heart, beginning on Nov. 1, 1933. After a very severe attack on Dec. 12 he was brought to the hospital. On that day the T-waves in Lead IV were 20 mm. high. Three days later the huge T-waves had disappeared.

CASE 7.—S. B. was a man of fifty-three years who had been well until Sept. 15, 1933. On that day while working as a "mattress maker," he noticed a heavy aching discomfort in both wrists, and a "queer" indescribable sensation in the lower substernal region. He sat down and the discomfort passed off in about an hour, leaving no noticeable after-effects. The next day at 11 A.M., he noticed a queer "jumping feeling" near the xiphoid. Soon the same heavy ache appeared in both wrists, and a severe pain developed in the lower sternal region. He felt weak, faint, and dizzy. The severe pain lasted two hours. After that it recurred each time he made the least physical effort. He did not go to bed. Since then he has had substernal pain on moderate effort, relieved by rest.

He was studied at the Mount Sinai Hospital from Oct. 25 to Dec. 7, 1933, on the service of Dr. Rubenstone. He had no fever, no leucocytosis, no abnormalities of heart sounds, and no evidence of congestive failure. The blood pressure was 125 mm. systolic and 70 mm. diastolic. A tonsillectomy was performed on Dec. 1, 1933.

He was seen by us on Jan. 27, 1934, through the kindness of Dr. Joseph Edeiken. His exercise tolerance had improved so that he could walk three blocks. The substernal pain induced by effort radiated to the right side of the chest and right shoulder, rather than to the left. The blood pressure was 130 mm. systolic and 80 mm. diastolic. There were no new physical signs. The orthodiagram showed slight enlargement of the left ventricle.

The electrocardiograms are shown in Fig. 7. The first tracing taken at Mount Sinai Hospital on Oct. 30, 1933, shows deeply inverted T-waves in Leads II and III. Lead IV shows a T-wave of normal size (–10 mm.). Lead V shows a T-wave of unusually large size (–19 mm.). Lead VI is similar to Lead III. The most recent tracing, taken Jan. 27, 1934, shows a disappearance of these large T-waves.

Summary: A man of fifty-three years suffered an attack of substernal pain on Sept. 16, 1933, lasting two hours. From that time on he has had effort angina, induced by slight exertion. On Oct. 30 an electrocardiogram showed T-waves in Lead V, 19 mm. deep, which returned to normal at a later date. In this case, the

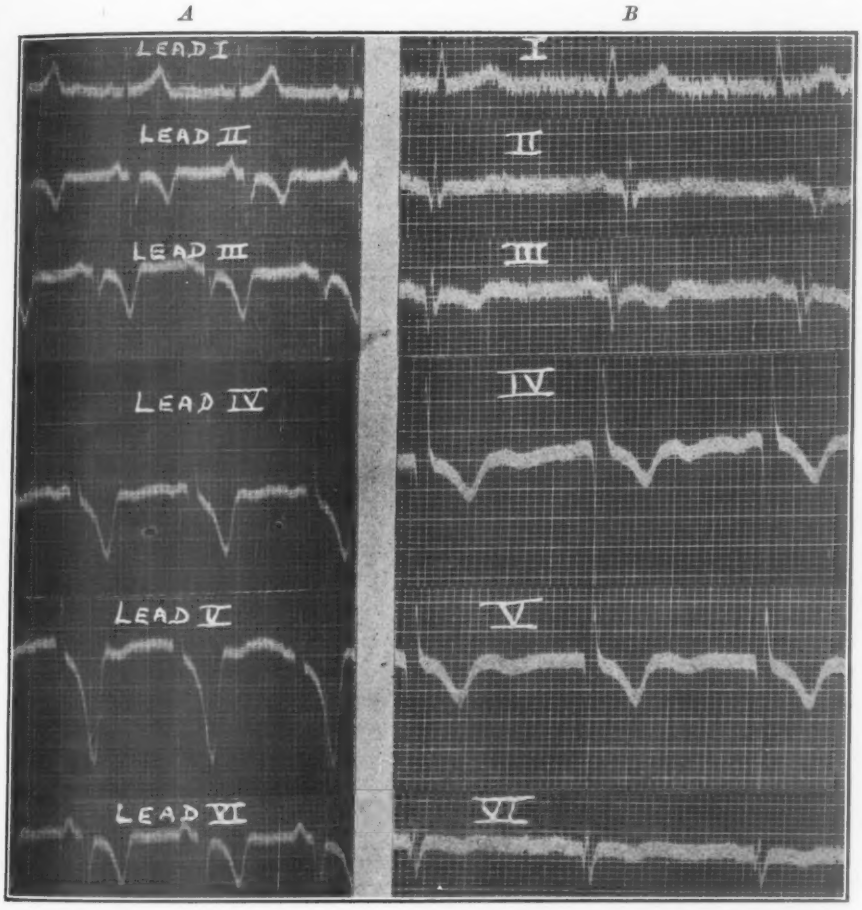

Fig. 7.—Electrocardiograms of Case 7. A moderately severe attack of substernal pain occurred Sept. 16, 1933. Since then the patient suffered recurring attacks of effort angina. Leads IV and V were taken with the anterior chest electrode at the apex impulse.

A, Tracing taken Oct. 30, six weeks after the onset. Lead I shows a large normal T-wave. Leads II and III show deep Q-waves and sharply inverted T-waves. Lead IV is quite normal. Lead V shows a huge inverted T-wave (-19 mm.). Lead VI resembles Lead III.

B, Tracing taken Jan. 27, 1934. The abnormally large T-waves have disappeared. The Q-waves in Leads II and III have persisted. T_2 is flat. Otherwise the tracing appears quite normal.

A T-wave in Lead V of -13 mm. has been seen in a presumably normal student. Consequently the large inverted T-wave in this case cannot be considered so distinctive as the large upright T-waves in Cases 1 to 6.

depth of the T-wave in Lead V is not necessarily diagnostic, though it does exceed any we have seen in normal individuals. However, the history, the changing electrocardiogram, and the characteristics of the limb lead tracings provide fairly good evidence of acute or subacute cardiac infarction.

DISCUSSION

Most of these cases with huge T-waves in Leads IV and V show T-waves of large amplitude in the limb leads. In certain cases, however, we have seen large T-waves in the limb leads without huge T-waves in Lead IV. This may have been due in some instances to the fact that the size of the T-wave in Lead IV varies markedly with the position of the anterior electrode in this group of cases. In Case 4, on Dec. 12, 1933 (Fig. 6 *A*), the T-wave in Lead IV was 18 mm. high when the anterior electrode was placed 4 cm. to the left of the apex impulse; yet it was only 5 mm. in amplitude, when this electrode was placed on the fourth left costal cartilage, 3 cm. from the sternum. In Case 6 on Dec. 12, 1933 (Fig. 6 *B*), T_4 was 20 mm. high with the anterior electrode in the third interspace, 4 cm. from the sternum; whereas it was only 8 mm. high with the anterior electrode 3 cm. to the left of the apex impulse. Therefore, it seems likely that huge T-waves might have been recorded in precordial leads of other cases showing large T-waves in the conventional leads, had the anterior electrode been placed in the position most favorable for recording this electrical disturbance. It seems probable that this "most favorable position" varies with the location of the infarct. The variation which occurs in the T-waves in precordial leads with variation in position of the anterior electrode, makes it important to interpret conservatively any changes which appear from day to day. Such changes might be due to alterations in relative position of the heart and anterior electrode, rather than alterations of the action current of the heart. When attempting to elicit huge T-waves, it is necessary to take the electrocardiogram from several different positions on the anterior wall of the chest.

Wilson and his coworkers[8] state that "since the anterior surface of the left chest is much closer to the heart than the posterior surface, anterior-posterior leads, used by Wolferth and Wood, are essentially precordial leads in which the indifferent electrode is placed on the back instead of upon the left leg." It would necessarily follow from this statement that Lead IV and Lead V taken without moving the anterior electrode are "essentially" the same. Although they are essentially the same in many individuals, particularly in normal individuals, there are certain cases in which Leads IV and V are quite different in contour. In Fig. 1 *A* of this paper, $T_4 = +18$ mm., $T_5 = +22$ mm. and $T_6 = +4$ mm. In Fig. 3 *B*, $T_4 = +24$, $T_5 = +18$, and $T_6 = -5$. In Fig. 4 *A*, $T_4 = +15$, $T_5 = +9$, and $T_6 = -6$. In Fig. 7 *A*, $T_4 = -10$, $T_5 = -19$, and $T_6 = -9$. These differences were not due to errors in

standardization of string deflection. In other words, when T_4 and T_6 deviate in opposite directions, T_5 is smaller than T_4. When T_4 and T_6 deviate in the same direction, T_5 is larger than T_4. The facts with regard to deviations of the RS-T interval seem to be similar. In a previous paper,[1] Chart 9 *B* shows a definite difference between the RS-T interval deviations in Leads IV and V, the latter being the larger. In this case RS-T_4 and RS-T_6 are both upright. On the other hand Chart 6 of the same paper shows the reverse relationship; i.e., a smaller RS-T interval deviation in Lead V than in Lead IV when RS-T_4 and RS-T_6 deviate in opposite directions. Therefore, both the RS-T interval and the T-wave appear to follow the same general rule, namely, that the amplitude of the deflection in Lead V seems to be approximately equal to the algebraic sum of the deflections in Leads IV and VI. It would seem, therefore, that although Leads IV and V often resemble one another, they not infrequently show marked differences and cannot be considered as substitutes for each other. Consequently, we are at present combining the technic of Wilson with our own. We are taking chest Leads IV, V, and VI with the anterior electrode at the apex; we then take Leads IV and V from two other points on the precordium, namely, (a) 4 cm. to the left of the apex impulse, and (b) over the body of the heart, 4 cm. to the left of the sternum. The use of this multitude of leads will probably not be found necessary for practical purposes in all cases. However, the tracings obtained are often so different (see Fig. 6) that it seems worth while to take them all for the present, especially in cases of acute coronary occlusion.

The appearance of the QRS complex in Leads IV and V in the group of patients with huge upright T-waves in the precordial leads is not constant. In three cases (2, 3, and 6) the initial downward deflection disappeared, as it frequently does in patients with infarction in the anterior surface of the left ventricle.[1] In the other cases the QRS complexes were bizarre. In four cases (1, 2, 3, and 4) at some time during their course a small upward deflection appeared before the initial downward deflection, giving a more or less M-shaped QRS. In a group of 250 presumably normal college students studied as a control series, only two showed a small upward deflection of QRS in Lead IV, prior to the downward deflection.[6] In neither of these was the deflection more than 1 mm. in amplitude. We therefore believe that a deflection of this type exceeding 2 mm. in height is a distinctly abnormal finding. It is seen most frequently in patients who have a history pointing to previous coronary occlusion. In some cases it seems to be a transition stage in the disappearance, or in the return of the initial downward deflection in Leads IV and V (cf., Case 2). The electrocardiogram of Case 1, taken thirteen months after the attack, was practically normal except for the presence of this wave.

At the time when huge upright T-waves appeared in Lead IV, three cases (2, 3, and 5) showed no deviation of the RS-T interval from the isoelectric line, one case (6) showed a depression of this interval, and two cases (1 and 4) showed an elevation.

The appearance time of these bizarre T-waves was not constant. They appeared in Case 6 on the day of the attack. On the other hand, they were absent in some cases (3 and 4) on the day of the attack, and appeared days or weeks later. Their time of disappearance also varied considerably. In Cases 2, 5, and 6, they disappeared rapidly within two or three days. However, in Case 4, they persisted for five or six weeks and disappeared after that time.

Although the patients in this group present the clinical picture of coronary occlusion, the symptoms and signs immediately associated with the huge T-waves are likely to be less severe than those recorded in the classical textbook description of this disease. Some of the patients have shown only slight fever and leucocytosis, and little or no fall of blood pressure. Two patients have died (Cases 2 and 5). In each instance, death occurred in a subsequent classical attack. In this connection Cooksey's observations[5] are of interest. He states that his cases with large T-waves in limb leads were suspected of having relatively small infarcts.

A rather striking clinical characteristic of this group of cases seems to be a liability to frequent recurrences of cardiac pain, for days or even weeks after the onset.

Only one case has come to necropsy (Case 2). In this patient the fatal lesion was a large infarct in the anterior surface of the left ventricle. There were no infarcts elsewhere in the heart. Examination of the coronary arteries suggested that several small coronary twigs in the anterior surface of the heart had been obstructed, prior to the fatal attack. With one exception (Case 5)* all the cases with huge upright T-waves in Leads IV and V presented electrocardiographic features more or less indicative of infarction in the anterior surface of the left ventricle.[1] The electrocardiogram of the case with the huge inverted T-wave in Lead V was the type usually associated with lesions in the posterior surface of the left ventricle.

The clinical picture presented by this group of patients and the changing electrocardiogram indicate that some acute or subacute disturbance of the blood supply of a part of the heart muscle is taking place. The relative mildness of the symptoms suggests that the lesion is either complete occlusion of a small coronary vessel or partial occlusion of a large one. The lesion associated with huge upright T-waves in precordial leads is probably located in the anterior surface of the left ventricle, in the distribution of the left anterior descending coronary artery. The lesion in Case 7, with a large inverted T-wave in Lead V,

*It is possible that this patient had several areas of infarction in the heart.

may have been in the posterior surface of the left ventricle. What the chemical change in the heart muscle may be, which causes this type of electrical response, is not known. Possibly it is a disturbance of the nutrition of the myocardial fibers which has not reached a degree sufficient to cause marked RS-T interval deviations.

SUMMARY

1. Seven cases are reported which show huge T-waves in the precordial leads of the electrocardiogram.

2. In all cases the large waves disappeared at a later date.

3. These huge T-waves are sometimes elicited from a small area of the precordium only. If the anterior electrode is placed elsewhere on the anterior chest wall, they may not appear in the tracing.

4. The symptoms in this group of cases point to the diagnosis of coronary occlusion. Their relative mildness suggests the complete occlusion of a small vessel or the partial occlusion of a large one.

5. The lesion associated with huge upright T-waves in precordial leads is probably located in the anterior surface of the left ventricle. The fact that this electrocardiographic phenomenon has not been seen in a series of 550 controls, makes it seem justifiable to regard it as indicative of an acute or subacute disturbance of the coronary circulation.

6. Large inverted T-waves in precordial leads considerably exceeding the normal amplitude probably signify the presence of a lesion in the posterior surface of the left ventricle, analogous to that causing huge upright T-waves.

7. RS-T interval deviations may be absent in this group of cases.

8. A small upward deflection, prior to the downward deflection of QRS in precordial leads, has been observed in several of these cases. This wave is probably an abnormal finding, if more than 2 mm. in height.

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Q AND T TYPES OF ELECTROCARDIOGRAMS: THEIR COMPARATIVE AND COMPLEMENTARY VALUE IN INDICATING OCCURRENCE OF ACUTE MYOCARDIAL INFARCTION*

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IN 1928, Parkinson and Bedford[2] reported a remarkable series of electrocardiographic tracings obtained following acute myocardial infarction. They found that the changes in the RS-T segment of the electrocardiogram fell into two groups which they designated as T_1 and T_3 types. Whitten and I[1] had arrived at a similar conclusion, and we accepted their nomenclature. The T_1 type of electrocardiogram is characterized in its earliest development by change of level and contour of the RS-T segment in Leads I and II, and a depression of the S-T interval in Lead III. The R-T interval in Leads I and II, but especially in Lead I, usually is elevated above the isoelectric line. The interval is likely to be convex, dome-shaped, or sloping downward toward the T-wave. Diphasic waves or T-waves of a monophasic type are common in the earliest stages. It is important to note that Leads I and III act conversely, so that elevation of the R-T segment in Lead I is opposed by depression of the S-T segment in Lead III. The changes in Lead II, although less in degree, frequently are seen to be similar to those in Lead I in cases of infarction in the anterior portion of the left ventricle. At a later stage, the monophasic or diphasic type of T-wave in Lead I or Leads I and II is replaced by frank inversion. The fact is noteworthy that, as the T-wave becomes inverted in Lead I, the T-wave in Lead III remains upright and becomes exaggerated and sharply peaked. Of particular significance in the later stages is the fact that the R-T segment arises at the isoelectric level, and often retains the rounded contour in Lead I or Leads I and II preceding the inverted T-wave. Pitfalls of interpretation will be avoided if one does not interpret RS-T segments in Lead I, which arise below the isoelectric level, as evidence of infarction. Conditions producing left ventricular strain are prone to produce a negative T-wave in Lead I with an S-T segment arising below the isoelectric level in the absence of myocardial infarction.

The T_3 pattern is characterized by precisely the opposite type of RS-T changes following acute myocardial infarction. In its early stages, the R-T segments are elevated in Leads II and III, and the S-T seg-

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ment is depressed in Lead I. A convex, dome-shaped, or sloping R-T segment preceding the T-wave is observed in Leads II and III. In the later stages, the R-T segment in Leads II and III tends to return to, and eventually reaches, the isoelectric level, and the depressed S-T segment in Lead I disappears. In this stage inversion of the T-wave in Leads II and III, with a rounded contour of the RS-T segment, is observed, whereas the T-wave in Lead I is upright, and becomes exaggerated and sharply peaked. Here again one must insist, in the later stages, that the R-T segment preceding the negative T-waves in Leads II and III arises on the isoelectric line, if the segment contours are to be regarded as evidence of a preceding acute myocardial infarction.

Wilson and his associates[3] recently described certain changes in the initial deflections of the ventricular complex in association with myo-

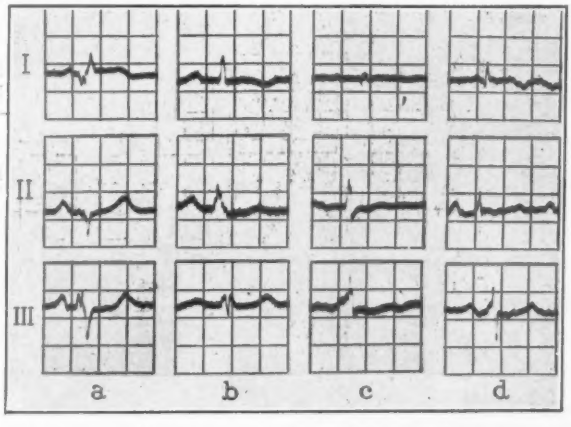

Fig. 1.—Four different patients. *a*, Electrocardiogram taken two days after acute coronary occlusion. Typical Q_1 and T_1 type. Necropsy disclosed acute and chronic infarction of the anterior and apical portion of the left ventricle. *b*, Electrocardiogram taken twenty-four hours after the onset of an attack of acute coronary occlusion. A fairly typical T_1 but no Q pattern is present. Necropsy was not performed. *c*, Electrocardiogram taken twelve weeks after an attack of acute coronary occlusion. The Q_1 type of change is definitely present and strongly supports the diagnosis of myocardial infarction. No R-T pattern can be recognized, probably because of the extreme low amplitude of all deflections in Lead I. *d*, Electrocardiogram taken two years after a typical attack of acute coronary occlusion. Necropsy disclosed ancient and recent infarction in the apex of the left ventricle. No history of recent acute occlusion was obtained. The T_1 pattern is probably present, but it is difficult to be sure of the characteristics of the R-T segment in Lead I. The presence of a fairly well developed Q_1 pattern greatly strengthened the diagnosis of myocardial infarction.

cardial infarction. They classified these changes under the headings of Q_1 and Q_3 types. They found the Q_1 type to be characterized by "the presence of a conspicuous and, in most instances, rather broad Q-wave in Lead I; the absence of Q in Leads II and III; the small amplitude of the largest of the initial deflections in Lead I, and the presence of a conspicuous S in Leads II and III." The Q_3 type is characterized by "the absence of Q in Lead I, the presence of a conspicuous Q in Leads II and III and the relatively small amplitude of the initial ventricular deflections in Lead II."

Since the publication of the article of Wilson and his associates, I have reviewed the 84 electrocardiograms taken of patients who have suffered from attacks of acute myocardial infarction. The diagnosis was based on good clinical evidence or proved at necropsy. It is apparent at once that the combined consideration of the Q and T types of electrocardiographic changes yields more information regarding infarction than does the consideration of either alone.

When a diagnosis of myocardial infarction was based only on clinical evidence, the Q and T patterns were equally characteristic in 18 cases; the Q_1 pattern more characteristic than the T_1 pattern in 6; the T_1 was more typical than the Q_1 type in 10; the Q_3 was more suggestive of acute infarction than the T_3 type in 6; the T_3 was more diagnostic than the Q_3 in 15; the Q_1 pattern of infarction was present in the absence

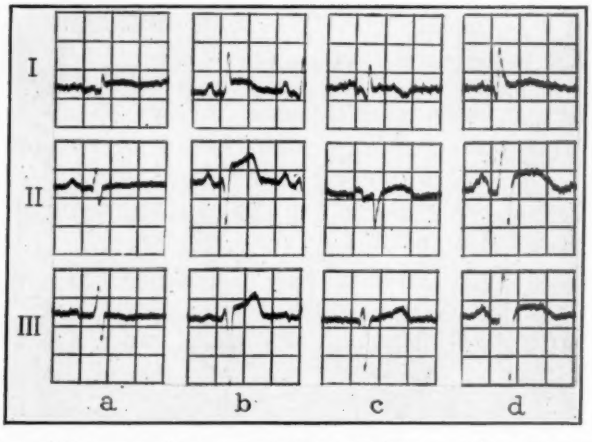

Fig. 2.—Three different patients. *a*, Electrocardiogram taken four months after acute coronary occlusion. Except for the high take-off of the R-T segment in Lead I, there is nothing in the RS-T segments to indicate previous myocardial infarction. The Q_1 pattern is typical, and confirms the diagnosis of infarction. The patient died four months later, but necropsy was not performed. *b*, Electrocardiogram taken two days after acute coronary occlusion. The elevation of the RS-T segments in all leads prevents the recognition of a definite T type of change. The Q_1 pattern is typical of acute myocardial infarction. This patient's infarction was complicated by acute pericarditis. *c*, Electrocardiogram of the same patient as the one represented in *b*, ten days later. Now a typical T_1 and Q_1 type of electrocardiogram is present. *d*, Electrocardiogram taken twenty-four hours after the onset of an attack of acute coronary occlusion complicated by acute pericarditis. The elevated RS-T segment in all leads prevents the classification of the electrocardiogram as a T type. The Q_1 pattern is typical of acute myocardial infarction.

of the T_1 pattern in 1; the T_1 pattern was present alone in 3; the Q_3 pattern occurred alone in none, and in 2 cases, the T_3 pattern was present in the absence of the Q_3 pattern.

When myocardial infarction was proved at necropsy, the Q and T patterns were equally positive in 11 cases; the Q_1 type was more typical than the T_1 type in 3; the T_1 was more characteristic than the Q_1 type in 1; the Q_3 pattern was more suggestive than the T_3 type in 4, and the T_3 pattern offered more evidence of cardiac infarction than the Q_3 pattern in 3.

There are several circumstances that account for the failure of the Q and T types to occur with equal clearness at a given time. In anterior apical infarction, the initial deflection of the electrocardiogram may have a very low amplitude. This so reduces the height of the R-T segment displacement that the change in level and contour of the segment and the inversion of the T-wave are all but unrecognizable. Under these conditions the Q_1 pattern may be present and easily recognizable. Likewise, in infarction in the posterior basal portion of the left ventricle, the amplitude of the initial ventricular deflection in Lead II may be small. On this account, changes in the level and contour of the R-T segment in this lead characteristic of a T_3 type may be difficult to recognize, and the presence of a Q_3 pattern may be of crucial importance. In certain instances infarction in the anterior apical portion of the left ventricle is followed by nothing more than slight rounding and upward displace-

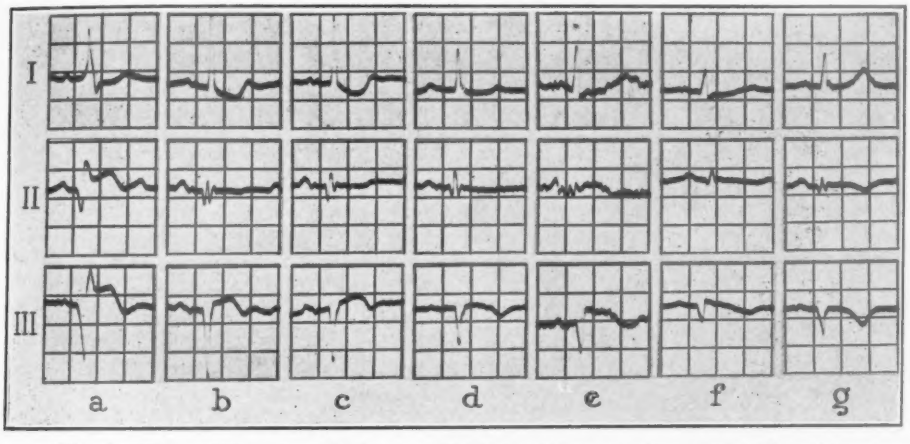

Fig. 3.—Three different patients. *a*, Electrocardiogram taken twenty-four hours after acute coronary occlusion. Typical T_3 and Q_3 patterns are present. Necropsy disclosed an acute infarction in the posterior basal portion of the left ventricle. *b*, Electrocardiogram taken two months after an attack of acute coronary occlusion. A typical Q_3 pattern is present. The RS-T segment changes suggest recent myocardial infarction, but Lead II does not participate in the usual manner. *c*, Tracing of the same patient as the one represented in *b*, one month later. The Q_3 pattern remains typical and diagnostic, but the RS-T in Lead II still does not conform to the usual T_3 type of change. *d*, Tracing taken on the same patient as the one represented in *b* and c, six weeks later. The Q_3 pattern remains far more convincing of myocardial infarction than does the T pattern, which now is practically unrecognizable. *e*, Electrocardiogram taken a few days after acute coronary occlusion. There is a typical T_3 type of change, except that the RS-T segment in Lead II is difficult to evaluate. The Q_3 pattern is typical and diagnostic of acute myocardial infarction. *f*, Tracing taken on the same patient as the one represented in *e*, seven days later. The Q_3 pattern is typically developed. The T_3 type still lacks the usual and typical R-T changes in Lead II, possibly owing in part to the low voltage of the deflections in that lead. *g*, Tracing taken on the same patient as the one represented in *e* and *f*, thirteen days later. The T_3 as well as the Q_3 pattern is now typical of recent acute myocardial infarction.

ment of the R-S segment in Lead I, without a corresponding depression of the S-T segment in Lead III. In this instance, the occurrence of a Q_1 pattern greatly strengthens the evidence of infarction.

Either the Q or T patterns may become positive first following acute infarction. They may remain as a relic of infarction equally long.

However, in some instances, the Q pattern may retain its identity longer than the T-pattern, as Wilson pointed out. In tracings under consideration at the clinic, this occurred occasionally, with the T_3 type of electrocardiogram at a stage when the R-T changes in Lead II had returned to normal.

Acute pericarditis complicating acute myocardial infarction frequently produces an anomalous type of electrocardiogram. This complication is prone to be followed by elevation of the RS-T segment in all leads, a picture which cannot be classed definitely as a T_1 or T_3 type of change. This situation may be greatly clarified if a definite Q pattern develops simultaneously.

The Q types of change may be confusing, and actually portions of Q_1 and Q_3 patterns may exist simultaneously in cases in which successive occlusions have occurred. The relic of a Q pattern from a healed acute

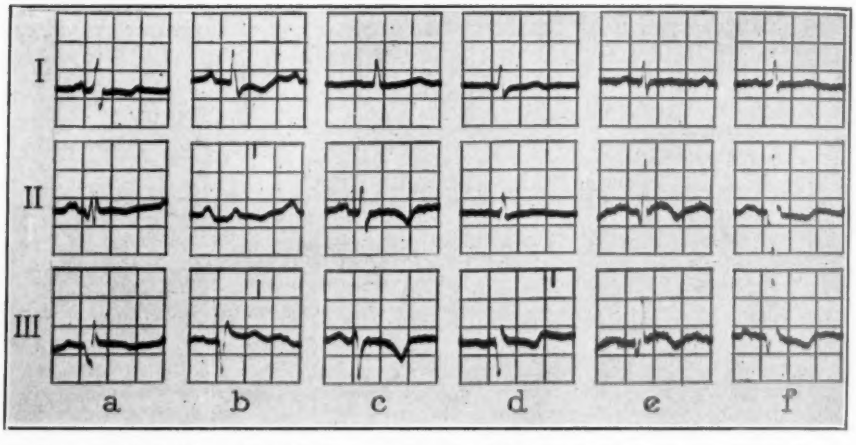

Fig. 4.—Five different patients. *a*, Electrocardiogram taken four months after an attack of acute coronary occlusion. The contour of the R-T segment in Lead III and the slight inversion of the T-wave in Lead II are slightly suggestive of ancient acute cardiac infarction. The presence of a typical Q_3 type of change in the initial deflections tremendously strengthens the diagnosis. *b*, Electrocardiogram taken after acute myocardial infarction. The time of coronary occlusion could not be obtained because the patient was in coma. There is a definite suggestion of a T_3 type of change. There is a typical Q_3, but no definite Q_2 deflection present. Necropsy disclosed acute infarction of the basal posterior half of the left ventricle. *c*, Electrocardiogram taken two weeks after an attack of acute coronary occlusion. A fairly typical late T_3 pattern of acute myocardial infarction is present, but a Q_3 pattern has not developed. *d*, Electrocardiogram taken two years and eight months after acute coronary occlusion. The electrocardiogram obtained at the time of occlusion showed a typical T_3 type of change. The present electrocardiogram has, as a relic of that event, an R-T segment in Lead III of the T_3 type. However, that change alone does not carry conviction of previous acute cardiac infarction. The Q_3 pattern is typically developed except for the absence of Q_2. The two patterns taken together constitute strong evidence of previous acute myocardial infarction. *e*, Electrocardiogram taken one week after acute coronary occlusion. The T_3 pattern is typically developed. The Q_3 pattern is atypical in that the initial deflection has its lowest amplitude in Lead I rather than in Lead II. *f*, Tracing taken on the same patient as the one represented in *e*, thirty-nine months later. The Q and T patterns have retained their original characteristics in about equal degree.

infarction may persist in some degree following a second infarction, leading to the development of a Q pattern approximating the opposite type. Here the T type of electrocardiogram may give more nearly unequivocal evidence of acute myocardial infarction than does the Q pattern.

And finally, acute myocardial infarction is followed at times by the development in the electrocardiogram of typical T patterns without the appearance of Q types of changes.

SUMMARY

Acute myocardial infarction is frequently followed by electrocardiographic changes that conform to both the Q and the T patterns indicative of such a condition. In general, the change in the RS-T segment is somewhat more likely to be typically developed and indicative of acute cardiac infarction than is the change in initial ventricular deflection, but occasionally the reverse is true. Not uncommonly neither type of electrocardiographic change is completely typical, but considered together they establish the presence of acute myocardial infarction. Only by such a combined study of the changes in the initial ventricular deflection and of the RS-T segment will one realize the full value of the electrocardiogram as a diagnostic aid.

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CORRELATION OF INITIAL DEFLECTIONS OF VENTRICULAR COMPLEX WITH SITUATION OF ACUTE MYOCARDIAL INFARCTION*

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WILSON and his associates described certain changes of the initial deflections of the ventricular complex of the electrocardiogram in association with myocardial infarction. They classified these changes under the headings of Q_1 and Q_3 types. They found the Q_1 type to be characterized by "the presence of a conspicuous and, in most instances, rather broad Q-wave in Lead I; the absence of Q in Leads II and III; the small amplitude of the largest of the initial deflections in Lead I, and the presence of a conspicuous S in Leads II and III." The Q_3 type is characterized by "the absence of Q in Lead I, the presence of a conspicuous Q in Leads II and III, and the relatively small amplitude of the initial ventricular deflections in Lead II." In discussing the relation the Q_1 and Q_3 types of electrocardiograms have to the location of the infarct, they concluded that although infarction in the anterior wall of the left ventricle and the adjacent septum generally was associated with a Q_1 type, yet at times it was associated with the Q_3 type. They described a Q_3 type of electrocardiogram of a patient in whom they found an infarct of the anterior portion of the left ventricle, but in whom later and more detailed examination of the heart disclosed the presence of an old and extensive infarct in the basal portion of the left ventricle. They did not state whether they considered that the latter finding accounted satisfactorily for the discordant electrocardiographic pattern which they reported.

I wish to present the data from 20 cases in which myocardial infarctions occurred and in which electrocardiograms conformed more or less closely to the Q_1 or Q_3 type. These data will appear, for the most part, in legends accompanying the illustrations. Necropsy was performed in all of these cases. In all but 3 cases, there was adequate evidence that acute coronary occlusions had occurred and in one of these 3 cases there was strong presumptive evidence that acute infarction had occurred.

In 7 cases in which electrocardiograms were typical or fairly typical Q_1 types, infarction in each instance was found in the anterior portion of the left ventricle and the adjacent septum. In each of these instances the Q_1 type of electrocardiogram was associated with changes in the tracing conforming more or less closely to the T_1 type.

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In 15 cases in which a Q_3 type of electrocardiogram was obtained, infarction in the posterior basal portion of the left ventricle was found in every instance. In each of these cases the Q_3 and T_3 types of change were present simultaneously.

One of the strongest reasons for believing that a uniform relationship exists between the Q pattern and the situation of infarction is afforded by 2 patients, each of whom suffered two successive acute infarctions; in each of the 2 cases a time interval elapsed and permitted adequate electrocardiographic studies after each infarction. Necropsy was performed on each of these patients. In the first case, acute infarction in the anterior portion of the left ventricle was followed by the development of a Q_1 T_1 type of electrocardiogram, and a second acute

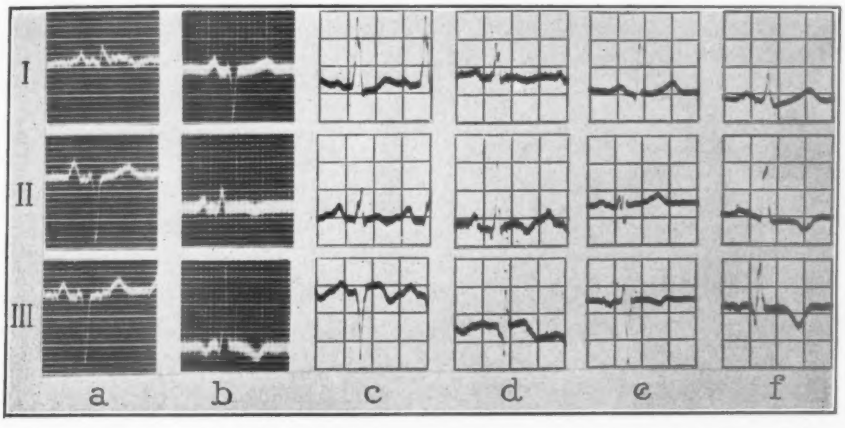

Fig. 1.—Electrocardiograms with shifting deflections. (Case 1) *a*, Q_1 type of electrocardiogram taken seventy-nine days after acute coronary occlusion. Necropsy disclosed ancient large infarction involving the apex, the anterior portion of the left ventricle, and the adjacent interventricular septum. *b*, Electrocardiogram of late T_3 type showing changes in the direction of the Q_3 type; that is, lowest amplitude of the QRS complex in Lead I in tracing *a* is replaced by lowest amplitude in Lead II; prominent S_3 is replaced by small Q_3, and Q_1 of tracing *a* has disappeared. Tracing *b* was made seven weeks after a second acute coronary occlusion. Necropsy disclosed subacute healing infarction in the posterior basal portion of the left ventricle. (Case 2) *c*, Q_3 type of electrocardiagram taken seventy-nine days after an attack of acute coronary occlusion. *d*, Electrocardiogram taken twenty-four hours after acute coronary occlusion showing a shift toward the Q_1 type. The Q-wave in Lead III is greatly diminished, and the QRS complex now has its smallest amplitude in Lead I. Necropsy was performed six days after the second occlusion and disclosed an old, practically healed infarction in the posterior basal portion, and a recent acute infarction in the anterior and apical portion of the left ventricle. (Case 3) *e*, Electrocardiogram taken one day before acute coronary occlusion. *f*, Electrocardiogram taken three days after acute coronary occlusion with changes tending toward the Q_3 type. Necropsy performed five days later disclosed thrombosis of the right coronary artery with extensive acute infarction in the posterior basal portion of the left ventricle and adjacent interventricular septum. There was an area of acute infarction in the anterior portion of the left ventricle measuring 1.5 cm. in diameter. This latter infarct may account for the fact that the latter tracing does not have a more prominent Q_2 and Q_3 and for the fact that the lowest amplitude of the QRS complex is in Lead I instead of in Lead II.

infarction in the posterior basal portion of the left ventricle caused a complete change of pattern to a late T_3 type and a picture approaching a Q_3 type (Fig. 1 *a* and *b*). That a typical Q_3 type was not reached may possibly be owing to the necessity for completely obliterating the previous Q_1 type. In the second case the order of these changes was

completely reversed; the first posterior basal infarct produced a Q_3 T_3 type of change, and the second infarction of the anterior portion of the left ventricle produced RS-T changes, definitely suggestive of a T_1 type of electrocardiogram, and changes in the initial ventricular complex in the direction of a Q_1 type (Fig. 1 *d* and *e*). These changes consist in the decrease in the size of S_3 and the subsequent appearance of the lowest amplitude of the QRS complex in Lead I, whereas previously this complex had its lowest amplitude in Lead II.

In a coordinate study,[4] I have pointed out that in acute myocardial infarction the T pattern of electrocardiographic changes may be present when the Q pattern is lacking, and vice versa. However, I have not encountered any case with a typical T_1 type of electrocardiogram in which a typical Q_3 pattern occurred, and I have observed no association of typical T_3 and Q_1 patterns. When anterior infarction succeeds posterior infarctions, an atypical Q_3 pattern may remain in association with a T_1 type of electrocardiogram, but the Q_3 pattern is atypical, and

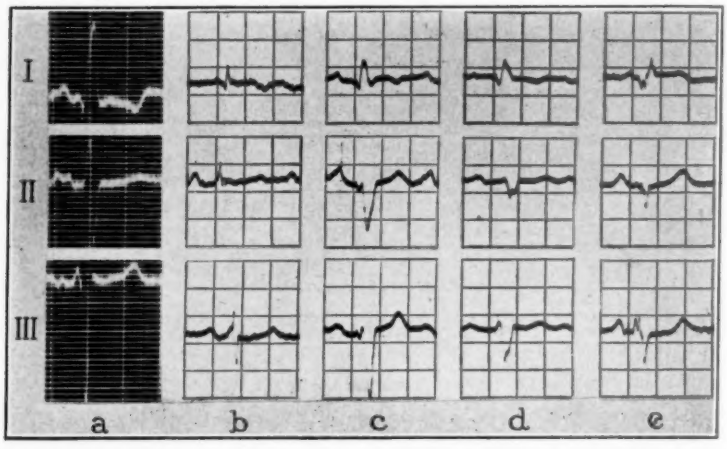

Fig. 2.—Initial deflections of the Q_1 type. (Case 4) *a*, Electrocardiogram conforming to the Q_1 type except that low amplitude of the QRS complex in Lead I is lacking. There was no history of acute coronary occlusion. The patient had hypertensive heart disease. Necropsy performed two months after this tracing was made disclosed high grade coronary sclerosis in all the vessels without occlusion. There were several fibrotic areas in the heart muscle in the region supplied by the anterior descending branch of the left coronary artery. A similar electrocardiogram is frequently obtained in hypertensive heart disease in the absence of coronary sclerosis or myocardial infarction. (Case 5) *b*, This electrocardiogram was obtained two years and three months after an attack of acute coronary occlusion. The patient died within twelve hours after this tracing was made. At necropsy, ancient and recent myocardial cardiac infarction was found in the apex and anterior portion of the left ventricle. (Case 6) *c*, This electrocardiogram was obtained fourteen months after an attack of acute coronary occlusion, and eighteen days before the patient's death. There was sclerosis of high degree through the distribution of the coronary artery, but the lumen was not completely occluded. The apex of the left ventricle was the site of a huge healed myocardial infarct. (Case 7) *d*, This electrocardiogram was taken three days before death. Death occurred suddenly, presumably the result of a thrombus which occluded the anterior descending branch at the level of origin of the circumflex branch of the left coronary artery. At necropsy the apex of the heart was thinned out and replaced by fibrous tissue, as was the adjacent interventricular septum. No history of ancient acute occlusion could be obtained. (Case 8) *e*, This electrocardiogram was taken two days after an attack of acute coronary occlusion, and two days before death. At necropsy, the apex and the adjacent anterior portion of the left ventricle and interventricular septum were found to be the site of acute and chronic myocardial infarction. There was aneurysmal dilatation at the apex with marked thinning of the wall of the heart in that region.

a careful study will show that it is veering definitely toward a Q_1 pattern. Wilson has called attention to a number of such published cases, of which the second case in this series, Case 2, is one. Case 1 shows that the same is true when posterior infarction follows anterior infarction, although the residue of the Q_1 pattern is less striking.

Granted that a typical Q_1 T_1 electrocardiographic pattern results from acute infarction in the anterior portion of the left ventricle, it does not follow necessarily that acute infarction in that area will lead to the development of the Q_1 T_1 type. The same may be said of infarction in the posterior basal portion of the left ventricle in respect to the Q_3 T_3 type of electrocardiogram. Extreme low voltage of the initial ventricular deflections, bundle-branch block, multiple acute infarcts involving both the anterior and the posterior portions of the left ventricle, massive widespread infarction, acute pericarditis or the effect of immi-

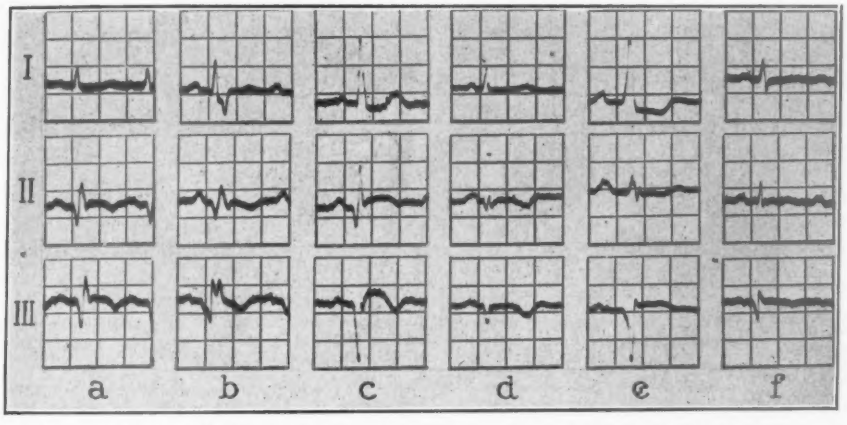

Fig. 3.—Initial deflections of the Q_3 type. (Case 9) *a*, This electrocardiogram was taken seven days after an attack of acute coronary occlusion and twelve days before death. At necropsy the right coronary artery was found to be occluded by a clot which could be seen projecting from its ostium. Acute myocardial infarction was present in the posterior portion of the left ventricle and extended to the apex. (Case 10) *b*, This electrocardiogram was taken one day after an attack of acute coronary occlusion and five days before the death of the patient. The QRS complex has a duration of 0.13 second. At necropsy an old infarct in the heart was found to occupy the lower third of the anterior portion of the interventricular septum. This had led to marked thinning and beginning aneurysm of the septum. The right coronary artery was sclerosed markedly and, 6 cm. from its orifice, was completely occluded. There was acute infarction in the posterior basal portion of the left ventricle, the posterior interventricular septum, and in the adjacent region of the right ventricle. This case well illustrates the predominating effect acute infarction exerts over chronic infarction in determining the type of Q T changes that result. (Case 11) *c*, This tracing was made four days after an attack of acute coronary occlusion and two days before the patient's death. At necropsy the descending branch of the right coronary artery was found to be occluded. There was acute myocardial infarction in the posterior portion of the left ventricle, the posterior interventricular septum, and in the adjacent portion of the right ventricle. (Case 12) *d*, This tracing was made twenty-four days before death. No history of acute coronary occlusion could be obtained. At necropsy there was extensive acute and subacute infarction in the posterior portion of the left ventricle extending from the apex almost to the base. The right coronary artery was sclerosed, grade 4, but no thrombus in the vessel could be demonstrated. (Case 13) *e*, This tracing was taken two months before death. No history of acute coronary occlusion could be obtained. At necropsy a large, fibrous scar was found, occupying the posterior basal portion of the left ventricle and extending in an attenuated projection around the interventricular septum toward its anterior third. (Case 14) *f*, This tracing was made one month before death. No history of acute coronary occlusion could be obtained. At necropsy the circumflex branch was found to be occluded by a thrombus. There was a soft area of infarction in the posterior portion of the left ventricle measuring 5 cm. by 6 cm.

nent death on a tracing may modify, obscure, or prevent the recognition of either the T or the Q patterns. Moreover, the electrocardiographic picture of acute myocardial infarction may be lost if electrocardiograms are not taken in sufficient number, or in proper time relation to acute coronary occlusion.

As Wilson and his associates pointed out, the pathological data and experimental evidence to date do not seem sufficient to attribute the development of the Q_1 type of electrocardiogram to block in the anterior subdivisions of the left branch of the bundle of His, nor to ascribe the Q_3 type to block in the posterior subdivisions of the bundle of His (Figs. 1, 2, 3, and 4).

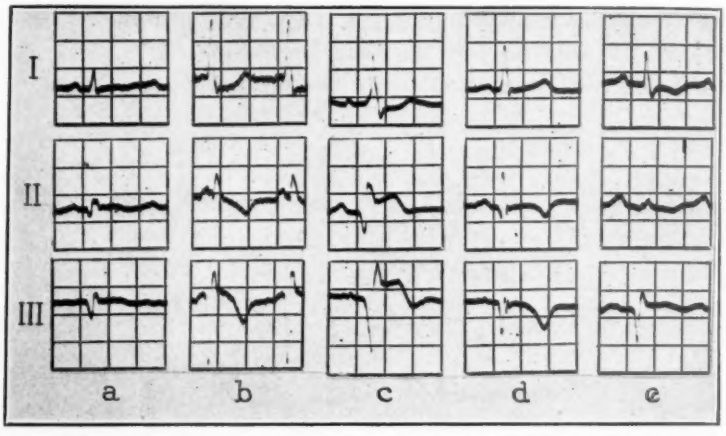

Fig. 4.—Initial deflections of the Q_3 type. (Case 15) *a*, This electrocardiogram was taken nineteen days after an attack of acute coronary occlusion and one day before the patient's death. At necropsy the circumflex branch of the left coronary artery was found to be occluded by a thrombus. The right coronary artery at a point 2 cm. distal to its orifice was nearly occluded. The posterolateral aspect of the left ventricle was the site of acute myocardial infarction. (Case 16) *b*, This tracing was made three days after an attack of acute coronary occlusion and two days before the patient's death. At necropsy an acute myocardial infarct was found to occupy the posterior portion of the left ventricle; it was 2 cm. in width and extended from the base to within 3 cm. of the apex of the left ventricle. (Case 17) *c*, This tracing was made one day following an attack of acute coronary occlusion and three days before the patient's death. At necropsy the left coronary artery was found to be almost occluded just below the point of origin of the circumflex. There was an old healed infarct situated in the anterior apical portion of the left ventricle. There was acute infarction in the posterior basal portion of the left ventricle extending down to and around the apex. The right coronary artery supplied all of the area of acute infarction, but no thrombus in the vessel was described in the original description of the dissection of the vessel. (Case 18) *d*, This tracing was taken one month following an attack of acute coronary occlusion and three years and ten months before the patient's death. Death occurred from acute coronary occlusion, but no tracing was obtained after the fatal attack. At necropsy an area of fibrosis was found in the posterior basal portion of the left ventricle without thinning of the wall. There was a large but scattered distribution of fibrous tissue in the endocardial half of the anterior portion of the left ventricle. (Case 19) *e*, The patient was in coma on admission and no history of coronary occlusion could be obtained. This tracing was taken two days before the patient's death. At necropsy a large area of acute infarction in the posterior half of the left ventricle was found. This area is supplied by the circumflex branch of the left coronary artery; the branch was occluded.

The electrocardiogram of Case 20 was too dim for photographic reproduction. It was of the Q_3 type, and at necropsy an area of healed infarction in the posterior wall of the left ventricle in the region supplied by the right coronary artery was found

CONCLUSIONS

1. The modifications of the initial ventricular deflections are correlated with the site of myocardial infarction.

2. Electrocardiograms typical of, or closely approximating, the typical Q_1 type are found to be associated with acute or healing acute infarction in the anterior and apical portion of the left ventricle and the adjacent interventricular septum.

3. The Q_3 type of electrocardiogram is found to be associated with acute or healing acute infarction in the posterior basal portion of the left ventricle and in the adjacent interventricular septum.

4. Not all acute infarctions in the left ventricle are followed by the characteristic Q patterns.

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ELECTROCARDIOGRAPHIC PATTERN OBSERVED FOLLOWING ACUTE CORONARY OCCLUSION COMPLICATED BY PERICARDITIS

Report of Cases*

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THE electrocardiogram taken following acute coronary occlusion has been of more assistance in the diagnosis of this disease than in that of any other cardiac lesion. Changes of the RS-T segment in the electrocardiogram occur that not only indicate the presence of acute myocardial infarction,[8] but also, under proper conditions,[1, 5] permit its localization in the heart before death. Changes in the initial deflection of the electrocardiogram have been described lately that, when typically developed, likewise indicate the occurrence of acute myocardial infarction[10] and have a definite localizing value.[2]

In attempting to evaluate electrocardiographic changes in cases in which acute coronary occlusion is suspected, the changes in the RS-T segment indicative of that condition may not be developed typically. As has been pointed out elsewhere, a combined study of the Q and RS-T patterns frequently will yield more information than a study of either pattern alone.[3]

The most characteristic feature of the RS-T segment changes following acute coronary occlusion is that an elevation of the R-T segment in Lead I is accompanied by a depression of the S-T segment in Lead III and vice versa. However, in some instances of infarction involving the anterior apical portion of the left ventricle, the only change that occurs in the RS-T segment in the first few days is elevation of the R-T segment in Lead I without a corresponding depression of the S-T segment in Lead III. This change, if the patient survives sufficiently long, usually is followed later by the development of a typical T_1 type of electrocardiogram. Another variation of the change in the RS-T segment following acute infarction consists in elevation or dome-shaped upward rounding of the RS-T segments in all leads. Obviously this change does not permit its classification as a T_1 or T_3 type, and yet the changing electrocardiogram is strong evidence of the acute coronary obstruction. Moreover, in its later stages, this electrocardiographic pattern is at times followed by inversion of the T-waves in all leads, which further complicates the attempt to classify the change as a T_1 or T_3 type. Evidence is submitted here to indicate that such an electrocardiogram is the result of acute coronary occlusion complicated by acute pericarditis.

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CASE 1.—A man, aged sixty years, was admitted to the hospital May 1, 1926. He was having a typical attack of coronary occlusion at the time of his admission. A definite pericardial friction rub was present on the second day. An electrocardiogram, taken seven days after his admission, showed an elevated take-off of the RS-T segment in each lead, the segments tending to have a definite dome shape (Fig. 1 *a*). A tracing taken two weeks later showed a definite inversion of the T-wave in Lead I of a Pardee type, and T_2 was now upright, peaked and exaggerated, a typical late T_1 type of electrocardiogram (Fig. 1 *b*). The patient recovered from this attack but died of pneumonia sixteen months later. At necropsy the anterior descending branch of the left coronary artery was found to be occluded in its lower third. Healed pericarditis completely obliterated the pericardial sac. The lower third of the anterior portion of the left ventricle and the adjacent portion of the interventricular septum were the site of an old infarction. There was marked thinning of the anterior and apical portions of the left ventricle with an organized thrombus beneath this area.

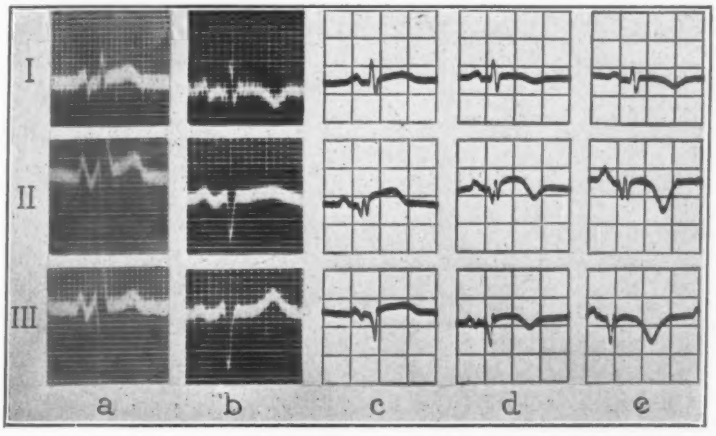

Fig. 1.—(Case 1) Standard electrocardiogram taken *a* seven days; and *b* twenty-one days after acute coronary occlusion; (Case 2) standard electrocardiogram taken *c* seven days, *d* eleven days, and *e* twenty-six days after acute coronary occlusion.

CASE 2.—A man, aged seventy-two years, was admitted June 21, 1929. Twenty-four hours previously he had been seized by an attack of acute epigastric pain which was still present on admission. On the day following, a definite pericardial friction rub was heard, and a diagnosis of acute coronary occlusion was made. The electrocardiogram taken on the seventh day showed an elevation and upward rounding of the RS-T segments in all leads without inversion of the T-waves (Fig. 1 *c*); a tracing taken four days later was similar except that the T-waves were inverted in all leads (Fig. 1 *d*). A third tracing, taken nineteen days after the first, showed a return of the S-T segments to the isoelectric level, with inversion of the T-waves in all leads (Fig. 1 *e*). At no stage could the electrocardiogram be classified as a T_1 or a T_2 type. The patient recovered from this attack and was allowed to go home. He was having marked symptoms of prostatic obstruction, and suprapubic cystostomy was performed October 30, 1929, which he withstood without incident. He died December 2, 1929, following suprapubic prostatectomy. At necropsy the pericardium was found to be adherent except over the posterior surface of the heart. The lower two-thirds of the anterior portion of the left ventricle were composed largely of scar tissue and were thin; the wall measured 0.8 cm. in thickness. The left coronary artery was sclerosed, graded 4.

That every patient in whom pericarditis complicates acute coronary occlusion does not have an electrocardiogram in which RS-T segments show elevation and upward rounding in all leads is shown by the following case.

CASE 3.—A man, aged sixty-seven years, had acute substernal pain and was admitted to the hospital as an emergency case. The electrocardiogram taken twenty-four hours after the onset of the pain showed slight elevation of R-T_1 with shallow inversion of the T-wave in that lead. The S-T segment in Lead II was slightly depressed (Fig. 2 *b*). Four days later a definite pericardial friction rub was present, and a tracing taken at that time did not show any additional changes (Fig. 2 *c*). The S-T segment in the fourth lead* in each of these tracings was distinctly elevated. The patient died on the seventh day of rupture of the heart at the site of acute infarction, with hemorrhage into the pericardium. At necropsy the anterior descending branch of the left coronary artery was found to be occluded

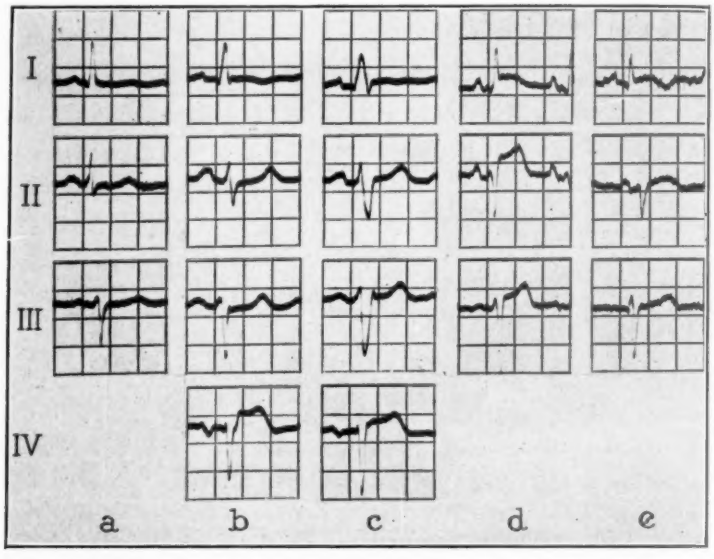

Fig. 2.—(Case 3) Standard electrocardiogram and the fourth lead taken *a* two and a half years before, *b* twenty-four hours after, and *c* five days after the onset of acute coronary occlusion; (Case 4) standard electrocardiogram taken *d* three days, and *e* thirteen days after the onset of acute coronary occlusion.

by a thrombus. A region over the apex of the heart and extending up into the anterior portion of the left ventricle, and measuring 8 cm. by 5 cm., was the site of acute infarction. This area was overlaid by a thick fibrinous blood-stained exudate. There was a recent fibrinous exudate over the base of the heart, extending well onto the great vessels.

In the fourth case the Q pattern indicated the site of infarction at a time when it could not be predicted from the character of the RS-T segments where the infarction would be found.

*In taking the fourth lead I have placed the left arm electrode on the anterior part of the thorax and the right arm electrode on the posterior part of the thorax. In tracings taken in this way the T-wave is normal when upright and abnormal when inverted. This application of the electrodes is opposite to that described and employed by Wolferth and Wood.

CASE 4.—A woman, aged sixty-nine years, suffering from chronic occlusive arterial disease of the legs, had an attack of acute coronary occlusion while under observation. A definite pericardial friction rub was heard three days after the onset of the attack. The electrocardiogram taken at that time showed elevation of the RS-T segments in all leads without inversion of the T-wave (Fig. 2 *d*). This electrocardiogram is a typical Q_1 type and is indicative of anterior apical infarction.[2] Daily electrocardiograms for the next five days showed no essential changes. The electrocardiogram taken thirteen days after the onset of acute coronary occlusion revealed RS-T changes that were now late typical manifestations of a T_1 type (Fig. 2 *e*) and indicated the anterior apical portion of the left ventricle as the site of infarction, as did the Q_1 pattern from the beginning. The patient made a satisfactory recovery and was dismissed from the hospital about one month after her attack.

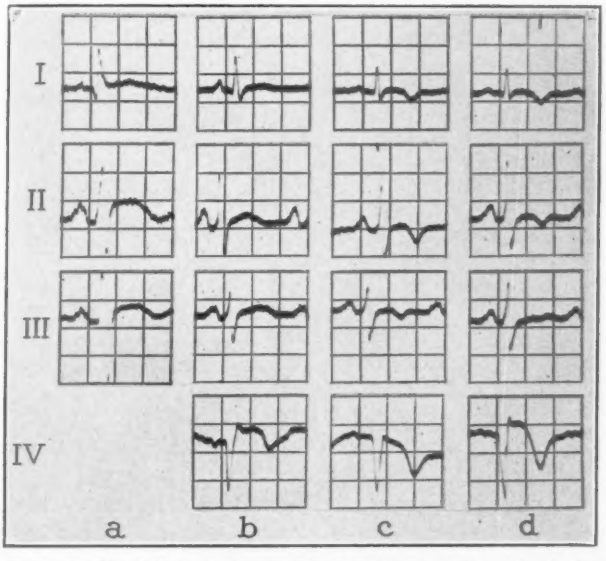

Fig. 3.—(Case 5) Standard electrocardiogram taken *a* the second day after acute coronary occlusion; (Case 6) standard electrocardiogram and the fourth lead taken *b* eight days after, *c* fourteen days after, and *d* thirty-five days after the onset of acute coronary occlusion.

CASE 5.—A man, aged fifty-seven years, suffered an acute attack of coronary occlusion, and a pericardial friction rub was audible on the day of the occlusion. Electrocardiograms were taken two and six days after this occlusion, and the tracings were practically identical. There was elevation or dome-shaped rounding of the RS-T segments in all leads. The Q_1 pattern was definitely present, indicative of anterior apical infarction[2] (Fig. 3 *a*). No further tracings were obtained. The patient's convalescence was uneventful, and he was dismissed from the hospital twenty-four days after the onset of occlusion.

CASE 6.—A man, aged sixty-one years, had an attack of acute coronary occlusion October 25, 1933, and was admitted to the hospital two days later. A pericardial friction rub was plainly audible on the second day. An electrocardiogram taken four days later showed upward rounding, but no elevation of the RS-T segments in all leads (Fig. 3 *b*). The S-T segment in the fourth lead was elevated and the T-wave was inverted. A tracing taken six days later showed definite inversions

of T-waves in all leads (Fig. 3 *c*). The electrocardiogram taken twenty-seven days after the first tracing showed a decrease of negativity of T_3, and the R-T segment in Leads I and II had become much more characteristic of a late T_1 type (Fig. 3 *d*). A typical Q_1 pattern now was present that indicated that the myocardial infarction had involved the anterior and apical portion of the left ventricle.[2] The patient's convalescence was uneventful, and he was dismissed from the hospital after thirty-four days of observation and treatment. The elevation of the S-T segment in the fourth lead was striking. Whether or not this is a feature confined to cases of acute myocardial infarction complicated by pericarditis, will require further study.

CASE 7.—A man, aged fifty-nine years, was admitted to the hospital in a typical attack of coronary occlusion. Two days later a definite pericardial friction rub was audible. An electrocardiogram obtained that day showed elevation of the RS-T segment in all leads (Fig. 4 *b*). A tracing taken twenty-one days after the second tracing showed inversion of all the T-waves and a Q_1 type of electrocardiogram

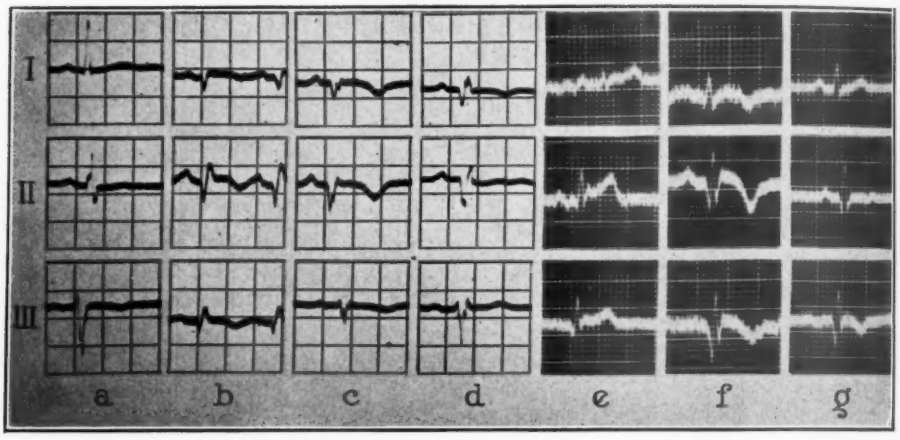

Fig. 4.—(Case 7) Standard electrocardiogram taken *a* three days before, *b* the day of, *c* twenty-one days after and *d* two years after acute coronary occlusion; (Case 8) standard electrocardiogram taken *e* forty-eight hours after, *f* eight days after, and *g* six months and eight days after the onset of acute coronary occlusion.

indicative of infarction of the anterior apical portion of the left ventricle (Fig. 4 *c*). In an electrocardiogram taken two years later, the T-wave in Lead III was upright, and the R-T segment in Lead I was a fairly typical late relic of a T_1 type of change (Fig. 4 *d*).

CASE 8.—A man, aged forty-eight years, was admitted during a severe attack of coronary occlusion, the pain lasting ninety-six hours. No friction rub was ever heard in this case. A tracing taken on the day of admission showed an elevated take-off of the RS-T segment in all leads (Fig. 4 *e*) with T-waves somewhat high in all leads but especially in Lead II. This tracing may be compared with that of a dog (Fig. 1 *d*) in the article by Mann and me following the reaction of the pericardium to operative injury. This type of tracing persisted for four days, and on the sixth day after admission the T-waves were negative in all leads (Fig. 4 *f*). Except for the fact that the initial deflection had its smallest amplitude in Lead I, this tracing could be classified as a Q_3 type indicative of infarction of the posterior basal portion of the left ventricle. A tracing taken six months

after the latter tracing showed the T-wave in Lead I upright, and it showed R-T segments in Leads II and III that were typical relics of ancient infarction in the posterior basal portion of the left ventricle (Fig. 4 *g*). In this case pericarditis was not observed clinically, yet these tracings resembled those previously shown when pericarditis was known to be a factor, and they suggested that that complication was present. No way exists of excluding from consideration infarction of both the posterior and the anterior portion of the left ventricle, in the original prolonged attack.

COMMENT

That pericarditis, complicating acute coronary occlusion in man, may modify the RS-T segments of the electrocardiogram in the foregoing manner receives support from other experimental and clinical data. Scott, Feil and Katz[9] recorded elevation of the RS-T segment in all leads in electrocardiograms of patients in whom sudden hydropericardium had developed. They reasoned that this electrocardiographic change resulted from hydrostatic pressure exerted on the heart and that it led to compression of the vascular channels and produced anoxemia, reduced cardiac output, and impaired coronary flow. They[7] were able to produce similar changes in the electrocardiograms of dogs by rapid distention of the pericardial sac with fluids. Barnes and Mann found that profound changes in the RS-T segment of the electrocardiogram occurred when the dog's pericardium was opened without molesting the coronary circulation. Subsequent necropsy of these animals indicated that extensive pericarditis followed this procedure. They believed that the modifications of the RS-T segment that followed resulted from the pericarditis. Fowler, Rathe and Smith observed similar changes in the electrocardiogram following production of pericarditis, and they demonstrated by microscopic study that the superficial layers of the myocardium were involved in the inflammatory process. They concluded it was this injury to the superficial layers of the myocardium that was responsible for the modifications in the electrocardiogram. There is no reason to suspect in the clinical cases presented here that pericardial effusion of any degree, or sudden in its accumulation, occurred. I am inclined to believe that the injury which the superficial layers of the myocardium sustain in the pericardial reaction accounts for the peculiar electrocardiographic change, an interpretation supported by the experiments just cited.

The types of electrocardiograms presented here have been difficult of interpretation heretofore. They could not be classed clearly as either of T_1 or T_3 type. Lacking this classification, they could not be utilized to predict the situation of the infarct. They were so bizarre that they sometimes led to the doubt as to whether there were electrocardiographic patterns of RS-T changes typical of acute cardiac infarction, inasmuch as they were encountered in the electrocardiograms of patients who were undoubtedly victims of acute coronary occlusion. True enough, the

changing character of the electrocardiogram indicated the presence of infarction, but the absence of the usual pattern was disturbing, none the less. I believe this study reveals the significance of this type of electrocardiogram, and the picture of elevation of the RS-T segment in all leads that occurs in a case of occlusion should lead to careful attempts to elicit a pericardial friction rub. Inasmuch as the friction rub may be heard only temporarily, the occurrence of this type of tracing strongly suggests the presence of pericarditis, even though evidence of its presence may otherwise escape the ear of the examiner.

It is further interesting to note that, except in Cases 1 and 8, there was some feature of the electrocardiograms that suggested that its character was dependent on infarction of the anterior and apical portions of the left ventricle. Whether infarction of the posterior basal portion of the left ventricle complicated by pericarditis can produce this picture, remains to be established by correlation of such electrocardiographic changes with cardiac pathology.

It is noteworthy that in some of these electrocardiograms, even though the RS-T pattern in its early form is distorted so as not to permit localization, the Q pattern is fully developed, and it indicates not only the presence but also the site of acute myocardial infarction.

CONCLUSIONS

The electrocardiograms of patients in whom acute coronary occlusion is complicated by pericarditis differ from the type of RS-T changes associated with uncomplicated, acute coronary occlusion. The typical feature of the electrocardiogram, seen in coronary occlusion associated with pericarditis in its early stages, consists of elevation or upward rounding of the RS-T segment in all leads. This may be followed by inversion of the T-wave in all leads. In some instances, it is followed by the development of a T pattern that can be classified definitely as a late relic of acute coronary occlusion. In the stage when the RS-T segment is elevated in all leads, the Q pattern may be typically developed, not only indicating infarction, but also pointing to the situation of the infarct in the left ventricle.

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THE VELOCITY OF PULMONARY AND PERIPHERAL VENOUS BLOOD FLOW AND RELATED ASPECTS OF THE CIRCULATION IN CARDIOVASCULAR DISEASE

Their Relation to Clinical Types of Circulatory Failure*

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THE velocity of blood flow in pathological states of the circulation is already well known. Investigations of recent years[1-6] have revealed a characteristic slowing of the blood flow in cardiovascular disease with circulatory failure, in myxedema and in polycythemia vera; and an acceleration of the circulation in thyrotoxicosis and anemia. In compensated heart disease, as well as in arterial hypertension and emphysema, the velocity of blood flow has been found to be normal or but slightly retarded.

Although concordant results have been obtained with the various methods employed, the radium emanation method[2] is particularly valuable in that it provides a separate estimation of the velocity of blood flow through the lungs and through the peripheral vascular areas. Such a differential index of the functional state of the greater and lesser circulations is of practical as well as theoretical value in the diagnosis and treatment of disorders of the circulation.

The cyanide method was devised in order to provide a simple, objective method for the separate measurement of the velocity of the pulmonary and of the peripheral venous blood flow in man. This method and the observations made in normal subjects were reported in a previous communication,[7] in which evidence was presented to show that sodium cyanide could safely be administered to man within a wide range of dosage, and that the cyanide "circulation time" was a reliable measure of the velocity of blood flow.

In order to ascertain whether the cyanide method would furnish a reliable measure of the velocity of blood flow in heart failure, measurements of the pulmonary circulation time, of the peripheral venous circulation time, and of other quantitative indices of the state of the pulmonary and the systemic circulations, as well as clinical observations, were made in patients with compensated heart disease and in patients with various degrees of circulatory failure. The pulmonary and venous circulation times obtained were then compared with those obtained with the

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radium emanation method in a group of subjects with similar clinical states. For a more precise evaluation, the cyanide and the dye or glucose circulation times were determined in the same person.

METHODS USED

The arterial pressure was determined with the aid of a mercury manometer; the venous pressure, by the direct venipuncture method of Moritz and von Tabora[8] with the arm resting at the level of the right auricle. In determinations of the vital capacity of the lungs, a calibrated spirometer was used. Measurements of the crude pulmonary circulation time and of the peripheral venous circulation time were made with the cyanide method in the usual manner[7]; in orthopneic, as in normal subjects, the antecubital injections were made with the arm resting at the level of the right auricle. Determinations of the dye (or glucose) arm-to-femoral circulation time were made with the vital red method of Hamilton and his associates,[9] in which the procedure is as follows: The subject reclines on his right side; the injection of dye is made into the antecubital vein of the elevated left arm; and the blood samples for colorimetric analysis are obtained by puncture of the femoral artery.

RESULTS

Measurements of the pulmonary and the peripheral venous circulation times, of the venous pressure and of the vital capacity were made in fifty-six patients with hypertensive, arteriosclerotic, syphilitic, or rheumatic heart disease. Of this group, forty-six were totally incapacitated and presented the symptoms and signs of circulatory failure while at rest; the remainder were ambulatory and without evidence of decompensation. The clinical observations and circulatory measurements are presented in Tables I to V, inclusive.

Patients With Cardiovascular Disease Without Circulatory Failure

No clinical evidence of circulatory failure could be detected in the ten patients with compensated heart disease (Table I), although in two instances (Cases 2 and 10) there was a history of circulatory failure. The vital capacity averaged 1,572 c.c. per square meter (980 to 2,100 c.c. per square meter), which is 34 per cent less than the average normal value of 2,376 c.c. per square meter[2]; the pulmonary circulation time, 13 seconds (10 to 15 seconds), or 23 per cent longer than the average normal (10.6 seconds)[7]; and the arm venous circulation time, 5.3 seconds (3 to 12 seconds), or 18 per cent longer than the average normal (4.5 seconds). The venous pressure was essentially normal, 7.7 cm. of water (5 to 10 cm.).

Except for the proportionately greater reduction in the vital capacity, these measurements lie within the normal range, although there is a tendency toward stasis and retardation of blood flow.

TABLE I

THE PULMONARY AND PERIPHERAL VENOUS CIRCULATION TIMES IN PATIENTS WITH CARDIOVASCULAR DISEASE WITHOUT CIRCULATORY FAILURE

CASE NO.	AGE	HEART RATE	ARTERIAL PRESSURE		VENOUS PRESSURE	VITAL CAPACITY		CYANIDE CIRCULATION TIME			DIAGNOSIS
			SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER	ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	yrs.	per min.	mm. Hg	mm. Hg	cm. H_2O	c.c.	c.c.	sec.	sec.	sec.	
1	59	96	165	110	+ 8	1600	980	13	10	3	Arterial hypertension; myocardial degeneration; emphysema.
2	23	78	150	35	–	3300	1800	16	11	5	Rheumatic heart disease; mitral stenosis and insufficiency; aortic stenosis and insufficiency.
3	56	84	125	80	–	2300	1190	20	12	8	Myocardial degeneration; emphysema.
4	35	92	100	65	+ 8	2850	1740	16	13	3	Rheumatic heart disease; mitral stenosis and insufficiency.
5	35	80	215	130	+ 8	3200	2100	25	13	12	Malignant hypertension.
6	57	78	140	80	+ 7	1800	1100	16	14	2	Myocardial degeneration; emphysema; arteriosclerosis.
7	49	60	120	75	+ 5	3250	1830	18	14	4	Myocardial degeneration; arteriosclerosis.
8	68	84	130	75	–	2200	1270	18	15	3	Myocardial degeneration; emphysema; arteriosclerosis.
9	66	58	170	75	–	3200	1840	22	15	7	Arterial hypertension; myocardial degeneration.
10	44	82	185	120	+10	3200	1870	19	–	–	Arterial hypertension; myocardial degeneration.
Average	49	79	150	84	+ 7.7	2690	1572	18.3	13	5.2	

Patients With Cardiovascular Disease With Circulatory Failure

Hypertensive Heart Disease.—Circulatory failure was present in seventeen patients with arterial hypertension and hypertensive heart disease (Table II). The majority of these patients suffered from paroxysmal cardiac dyspnea. They all exhibited orthopnea and other clinical signs of pulmonary stasis[10]; whereas only approximately one-half of them showed peripheral edema. None showed cardiac arrhythmia.

These patients with circulatory failure are divided into two groups: Group A, showing failure of the pulmonary circulation only; and Group B, showing failure of the entire circulation. In the nine patients of Group A, the vital capacity ranged between 550 and 1,640 c.c. per square meter, with an average of 1,049 c.c., which is 56 per cent below normal. The pulmonary circulation time varied between 13 and 22 seconds, averaging 16.8 seconds, or 58 per cent longer than the normal time. The arm venous circulation time, on the other hand, varied between 2 and 8 seconds, with an average of 4.1 seconds, which is 9 per cent *shorter* than the normal time. The venous pressure was essentially normal, averaging 8.2 cm. of water (6 to 11 cm.).

Subsequent observations made in Cases 3, 5, 6 and 7 (Table II) after slight to moderate clinical improvement had occurred, revealed an increase in average vital capacity from 968 to 1,440 c.c. per square meter; a decrease in the pulmonary circulation time from 17 to 15.5 seconds, and in the venous circulation time from 4.2 to 3 seconds; and a lowering of the venous pressure from 9.5 to 6.8 cm. of water. In the four subjects (Cases 2, 7, 8, 9) who subsequently showed more advanced circulatory failure, on the other hand, there was a decrease in the average vital capacity from 1,238 to 1,093 c.c. per square meter; an increase in the pulmonary circulation time from 17.5 to 22.5 seconds, and in the venous circulation time from 3.5 to 4.5 seconds; and an elevation of the venous pressure from 7.5 to 11.8 cm. of water. Thus, coincident with clinical improvement there was a tendency toward a return to normal in these aspects of the circulation; whereas with more advanced failure, a further deviation from normal occurred.

In the eight patients of Group B who exhibited failure of both pulmonary and peripheral circulations the vital capacity averaged 1,055 c.c. per square meter (700 to 1,310 c.c.), or 56 per cent less than normal. Both the pulmonary and the peripheral circulation times were increased, the pulmonary circulation time to an average of 22.5 seconds (13 to 35 seconds), or 112 per cent longer than the normal time, and the arm venous circulation time to 8.8 seconds (2 to 25 seconds), or 96 per cent longer. The venous pressure, averaging 16.3 cm. of water (11 to 23 cm.), was 123 per cent greater than the average normal pressure.[2]

Four subjects of Group B (Cases 12, 15, 16, 17) subsequently showed moderate clinical improvement, with the disappearance of peripheral

TABLE II

THE PULMONARY AND PERIPHERAL VENOUS CIRCULATION TIMES IN PATIENTS WITH HYPERTENSIVE HEART DISEASE WITH CIRCULATORY FAILURE

CASE NO.	AGE	DATE	HEART RATE	ARTERIAL PRESSURE		VENOUS PRESSURE	VITAL CAPACITY		DYE CIRCULATION TIME ARM TO FEMORAL	CYANIDE CIRCULATION TIME			REMARKS
				SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER		ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	YEARS		PER MIN.	MM. HG	MM. HG	CM. H_2O	C.C.	C.C.	SEC.	SEC.	SEC.	SEC.	
Group A. Patients with failure of the pulmonary circulation and normal peripheral circulation													
1	49	4/20/31	108	210	120	8	1500	970	15*	15	13	2	Marked failure. Intense dyspnea. Orthopnea 40°. Edema 0. Died 4 days later.
2	25	6/29/31	100	175	125	6	1800	1260	–	17	13	4	Malignant hypertension. Mild circulatory failure. Orthopnea 20°. Edema 0.
		8/18/31	104	235	160	14	950	660	–	21	18	3	Condition worse. Orthopnea 40°. Edema 1+. Died 2 months later.
3	52	4/29/32	96	210	115	10	1750	1110	15	16	14	2	Uremia. Intense dyspnea at rest. Orthopnea 25°. Edema 0.
		5/13/32	84	195	95	7	2140	1350	16	17	14	3	Slight improvement. Dyspnea on slight exertion. Orthopnea 0°. Edema 0.
4	56	1/12/31	94	170	110	6	–	–	–	22	15	7	Moderate failure. No dyspnea at rest. Orthopnea 45°. Edema 0.
5	60	9/23/31	92	160	85	9	1000	550	19	24	16	8	Moderate failure. Orthopnea 40°. Edema 0.
		11/ 5/31	72	160	85	4	2150	1180	–	19	14	5	Moderate improvement. Orthopnea 15°. Edema 0. Died 6 weeks later.

*Glucose circulation time.

TABLE II—CONT'D

CASE NO.	AGE	DATE	HEART RATE	ARTERIAL PRESSURE		VENOUS PRESSURE	VITAL CAPACITY		DYE CIRCULATION TIME ARM TO FEMORAL	CYANIDE CIRCULATION TIME			REMARKS
				SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER		ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	YEARS		PER MIN.	MM. HG	MM. HG	CM. H_2O	C.C.	C.C.	SEC.	SEC.	SEC.	SEC.	
6	62	4/24/31	76	220	110	8	2600	1360	18*	21	19	2	Mild failure. Dyspnea on slight exertion. No orthopnea nor edema.
		5/ 7/31	62	210	95	8	3500	1830	–	20	19	1	Improved. Dyspnea on moderate exertion.
7	71	11/19/31	64	220	100	11	1500	850	23	24	19	5	Moderate failure. Orthopnea 30°. Edema 0.
		11/30/31	72	220	90	8	2500	1400	–	18	15	3	Improved. Orthopnea 15°. Edema 0. No dyspnea.
		1/ 8/32	80	210	105	7	2250	1280	24	21	19	2	Condition worse. Orthopnea 25°. Edema 0. Died 5 weeks later.
8	57	4/ 8/31	72	155	95	6	2700	1640	24*	24	20	4	Frequent attacks of paroxysmal dyspnea. Orthopnea 45°. Edema 0.
		5/29/31	72	155	105	10	2600	1580	–	40	33	7	Condition worse. Continuous dyspnea. Frequent attacks of paroxysmal dyspnea. Edema 1+. Died 2 weeks later.
9	56	4/20/31	100	220	145	10	1300	650	24*	25	22	3	Uremia. Intense dyspnea. Orthopnea 30°. Edema 0.
		5/ 8/31	82	250	145	16	1700	850	–	26	20	6	Condition worse. Orthopnea 0°. Edema 1+.
Group B. Patients with failure of both pulmonary and peripheral circulations													
10	42	6/15/32	114	212	156	15	2630	–	–	15	13	2	Congestive failure. Intense dyspnea. Orthopnea 70°. Edema 3+.
11	63	3/28/31	70	180	105	11	2750	1310	–	25	17	8	Arteriosclerosis. Moderate decompensation. Orthopnea 30°. Edema 1+.

*Glucose circulation time.

TABLE II—CONT'D

CASE NO.	AGE	DATE	HEART RATE	ARTERIAL PRESSURE		VENOUS PRESSURE	VITAL CAPACITY		DYE CIRCULATION TIME ARM TO FEMORAL	CYANIDE CIRCULATION TIME			REMARKS
				SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER		ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	YEARS		PER MIN.	MM. HG	MM. HG	CM. H_2O	C.C.	C.C.	SEC.	SEC.	SEC.	SEC.	
12	50	5/28/31	90	165	95	12	1200	700	–	23	19	4	Mild asthmatic seizure. Orthopnea 40°. Edema 2+.
		6/18/31	80	150	80	8	–	–	21	24	20	4	Moderate improvement. No orthopnea nor edema.
13	60	10/29/31	84	240	130	17	–	–	–	26	20	6	Uremia. Marked Cheyne-Stokes' respiration. Orthopnea 20°. Edema 4+. Died.
14	57	10/ 2/31	68	160	100	17	1300	740	36	40	24	16	Advanced failure. Orthopnea 60°. Edema 3+.
15	54	9/25/31	104	195	150	23	2200	1250	24	30	26	4	Uremia. Orthopnea 15°. Edema 1+.
		10/ 1/31	84	195	125	14	2350	1330	18	22	17	5	Moderate improvement. Died 2 weeks later.
16	46	10/ 8/31	84	180	95	17	2550	1260	28	31	26	5	Severe failure. Orthopnea 45°. Edema 2+. Cheyne-Stokes' respiration.
		11/ 7/31	84	160	115	7	3320	1700	25	25	18	7	Improved. Orthopnea 15°. Edema 0.
		11/ 5/31	84	170	110	9	3250	1650	28	30	23	7	Slightly worse. Orthopnea 20°. Edema 0. Died 8 months later.
17	68	3/14/31	72	170	115	18	1800	1070	–	60	35	25	Severe failure. Orthopnea 60°. Anasarca. Cheyne-Stokes' respiration.
		4/15/31	60	150	95	7	3000	1770	36*	35	27	8	Moderate improvement. Slight orthopnea. Edema 0.

*Glucose circulation time.

edema and either improvement or disappearance of orthopnea. The average vital capacity was increased from 1,070 to 1,600 c.c. per square meter; the pulmonary circulation time was shortened from 26.5 to 20.5 seconds; and the venous pressure was lowered from 17.5 to 9.5 cm. of water. In the one instance with retarded venous circulation, the circulation time decreased from 25 to 8 seconds. Following a transient period of improvement Case 16 became more severely decompensated; coincidently the pulmonary circulation time was prolonged from 18 to 23 seconds, but the vital capacity and other aspects of the circulation showed no change.

Arteriosclerotic Heart Disease.—The observations made in eleven patients with generalized arteriosclerosis, myocardial degeneration and circulatory failure are presented in Table III. There was no evidence of antecedent arterial hypertension in any of these patients. In two cases the blood pressure was temporarily elevated during congestive failure, but it returned to normal with clinical improvement. All the members of this group exhibited orthopnea and cyanosis, and they all suffered from chronic pulmonary emphysema as well as from myocardial disease.

Six patients (Group A) showed clinical evidence of failure of the pulmonary circulation without peripheral circulatory abnormality. The average vital capacity was 968 c.c. per square meter (710 to 1,170 c.c.), or 59 per cent below normal; the pulmonary circulation time, 22.3 seconds (15 to 33 seconds), or 110 per cent longer than the normal time; the venous circulation time, 6.7 seconds (3 to 14 seconds), or 49 per cent longer than the normal time; and the venous pressure, 6.7 cm. of water (3 to 11 cm.), or essentially normal. Coincident with clinical improvement in three cases (Cases 2, 4, 5), there was a considerable increase in the vital capacity (1,000 to 1,533 c.c. per square meter), and a decrease in the pulmonary circulation time (22.3 to 17.7 seconds), but no significant change in the previously normal venous circulation time (5.3 to 5 seconds) or in the venous pressure (7.7 to 5.7 cm. of water).

In five patients (Group B) in whom there was failure of both the pulmonary and the peripheral venous circulations, the vital capacity varied between 680 and 1,310 c.c. per square meter, with an average value of 975 c.c., or a reduction of 59 per cent; the pulmonary circulation time ranged from 22 to 45 seconds, with an average of 28 seconds, or a prolongation of 162 per cent; the venous circulation time measured from 2 to 20 seconds, with an average of 9.8 seconds, or a prolongation of 112 per cent; and the venous pressure varied between 7 and 20 cm. of water, with an average of 14.6 cm., or an increase of 100 per cent. Clinical improvement occurred in all of these patients, and coincidently there was an increase in the vital capacity from 975 to 1,315 c.c. per square meter; a decrease in the pulmonary circulation time from 28 to 19.2 seconds, and in the venous circulation time from 9.8 to 6.2 seconds; and a decrease in the venous pressure from 14.6 to 5.4 cm. of water.

TABLE III

THE PULMONARY AND PERIPHERAL VENOUS CIRCULATION TIMES IN PATIENTS WITH ARTERIOSCLEROTIC HEART DISEASE WITH CIRCULATORY FAILURE

CASE NO.	AGE	DATE	HEART RATE	ARTERIAL PRESSURE		VENOUS PRESSURE	VITAL CAPACITY		DYE CIRCULATION TIME ARM TO FEMORAL	CYANIDE CIRCULATION TIME			REMARKS
				SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER		ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	YRS.		PER MIN.	MM. HG	MM. HG	CM. H_2O	C.C.	C.C.	SEC.	SEC.	SEC.	SEC.	
Group A. Patients with failure of the pulmonary circulation and normal peripheral circulation													
1	57	6/6/31	96	125	95	3	1400	720	16	20	15	5	Marked emphysema. Intense dyspnea. Orthopnea 40°. Edema 0. Died 3 months later.
2	58	5/ 8/31	90	145	85	8	1500	710	18	21	18	3	Mild attack of paroxysmal dyspnea. Auricular fibrillation. Orthopnea 45°. Edema 0.
		6/23/31	92	100	70	6	2850	1360	17	17	15	2	Moderate improvement. Orthopnea 20°. Edema 0.
3	73	4/29/31	96	125	78	11	–	–	–	24	19	5	Moderate failure. Orthopnea 30°. Edema 0.
4	68	10/ 9/31	84	140	90	5	2100	1170	30	28	21	7	Moderate failure. Orthopnea 35°. Edema 0.
		10/30/31	68	135	75	6	3500	1940	21	24	18	6	Marked improvement. Ambulatory. Orthopnea 0°. Edema 0.
5	71	3/14/31	64	110	55	10	1900	1120	–	34	28	6	Emphysema. Mild failure. Orthopnea 15°. Edema 0.
		3/27/31	64	110	50	5	2200	1300	–	27	20	7	Moderate improvement. Orthopnea 10°.
6	63	6/ 6/31	108	125	95	3	2300	1120	–	47	33	14	Mild failure. Healed cardiac infarct. Auricular fibrillation. Orthopnea 35°. Edema 0.

TABLE III—CONT'D

CASE NO.	AGE	DATE	HEART RATE	ARTERIAL PRESSURE		VENOUS PRESSURE	VITAL CAPACITY		DYE CIRCULATION TIME ARM TO FEMORAL	CYANIDE CIRCULATION TIME			REMARKS
				SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER		ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	YRS.		PER MIN.	MM. HG	MM. HG	CM. H_2O	C.C.	C.C.	SEC.	SEC.	SEC.	SEC.	
Group B. Patients with failure of both pulmonary and peripheral circulations													
7	63	12/ 7/32	104	170	105	17	1400	700	26	24	22	2	Severe failure. Cheyne-Stokes' respiration. Orthopnea 60°. Edema 3+.
		12/31/32	84	155	95	2	2300	1150	22	22	19	3	Slight improvement. Orthopnea 20°. Edema 1+. Died 5 months later.
8	46	3/17/32	146	100	90	17	2520	1310	27	27	24	3	Intense dyspnea. Orthopnea 50°. Edema 0. Auricular fibrillation.
		3/24/32	82	110	80	6	3800	1990	22	23	19	4	Moderate improvement. Auricular fibrillation. Orthopnea 20°. Died suddenly 3 weeks later.
9	80	1/14/32	80	150	100	12	1190	680	37	33	24	9	Advanced failure. Auricular fibrillation. Intense dyspnea. Orthopnea 30°. Edema 4+.
		1/16/32	72	125	65	7	1240	710	31	30	19	11	Slight improvement. Orthopnea 20°. Edema 3+. Died suddenly 2 days later.
10	64	4/ 3/31	80	140	90	7	–	–	–	40	25	15	Severe failure. Cheyne-Stokes' respiration. Auricular fibrillation. Orthopnea 80°. Edema 1+.
		4/22/31	68	110	75	5	2000	1150	28*	26	21	5	Moderate improvement. Mild periodic breathing. Orthopnea 20°. Edema 0.
11	70	2/11/32	144	100	80	20	2000	1210	–	65	45	20	Severe failure. Auricular fibrillation. Cheyne-Stokes' respiration. Orthopnea 25°. Edema 4+.
		2/19/32	70	120	75	7	2350	1410	20	26	18	8	Marked improvement. Chest clear. No orthopnea nor edema.

*Glucose circulation time.

TABLE IV

THE PULMONARY AND PERIPHERAL VENOUS CIRCULATION TIMES IN SYPHILITIC HEART DISEASE WITH CIRCULATORY FAILURE

CASE NO.	AGE	DATE	HEART RATE	ARTERIAL PRESSURE		VENOUS PRESSURE	VITAL CAPACITY		DYE CIRCULATION TIME ARM TO FEMORAL	CYANIDE CIRCULATION TIME			REMARKS
				SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER		ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	YEARS		PER MIN.	MM. HG	MM. HG	CM. H_2O	C.C.	C.C.	SEC.	SEC.	SEC.	SEC.	
Group A. Patients with failure of the pulmonary circulation and normal peripheral circulation													
1	33	6/ 2/32	104	160	45	8	800	450	15	17	14	3	Aortic regurgitation. Intense dyspnea. Orthopnea 80°. Edema 0. Died 5 days later.
2	56	11/14/32	100	210	50	8	2500	1470	–	24	20	4	Aortic regurgitation. Moderate failure. Orthopnea 30°. Edema 0.
3	41	10/30/31	100	125	50	9	1300	875	–	31	23	8	Aortic regurgitation. Coronary disease. Advanced failure. Orthopnea 40°. Edema 0. Died 8 months later.
4	54	3/16/31	76	185	50	11	1800	1010	–	35	27	8	Aortic regurgitation. Aneurysm. Dyspnea on slight exertion. No orthopnea nor edema.

TABLE IV—CONT'D

CASE NO.	AGE	DATE	HEART RATE	PRESSURE ARTERIAL		VENOUS PRESSURE	VITAL CAPACITY		DYE CIRCULATION TIME ARM TO FEMORAL	CYANIDE CIRCULATION TIME			REMARKS
				SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER		ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	YEARS		PER MIN.	MM. HG	MM. HG	CM. H_2O	C.C.	C.C.	SEC.	SEC.	SEC.	SEC.	
Group B. Patients with failure of both pulmonary and peripheral circulations													
5	49	3/ 6/32	72	105	65	19	2500	1440	23	35	22	13	Aortic regurgitation. Aneurysm. Moderate failure. Orthopnea 40°. Edema 1+.
6	61	5/ 9/31	104	110	65	6	1600	1065	–	31	24	7	Aortitis. Coronary occlusion. Moderate failure. Slight dyspnea. Orthopnea 10°. Edema 1+. Died suddenly 12 hours later.
7	52	6/ 7/32	92	158	55	19	2330	1455	30	34	26	8	Aortic regurgitation. Aneurysm. Advanced failure. Slight dyspnea. Orthopnea 25°. Edema 3+.
		6/18/32	96	175	40	13	2400	1500	34	37	27	10	No change. Died 6 weeks later.
8	49	11/11/31	168	120	95	27	–	–	–	42	36	6	Aortic aneurysm. Auricular fibrillation. Intense dyspnea. Orthopnea 90°. Edema 0.
		11/11/31	104	110	95	25	–	–	–	42	–	–	Two hours later moderate improvement. Orthopnea 60°. Edema 0. Died 2 days later.
9	46	6/13/32	108	104	74	12	1650	1000	–	54	43	11	Aortitis with coronary disease. Paroxysmal dyspnea. Advanced failure. Moderate dyspnea. Orthopnea 30°. Edema 3+.
		10/21/32	108	108	76	–	–	–	68	65	–	–	Condition worse. Intense dyspnea. Cheyne-Stokes' respiration. Orthopnea 45°. Edema 2+. Died 24 hours later.

Syphilitic Heart Disease.—The nine patients with syphilitic heart disease suffered from paroxysmal cardiac dyspnea and showed the signs and symptoms of circulatory failure. As indicated in Table IV, aortic insufficiency was present in six of these patients, aortic aneurysm in four, and both of these lesions in three. In two patients (Cases 6 and 9) who exhibited no clinical or roentgen-ray evidence of aneurysm or aortic valve disease, syphilitic aortitis with almost complete occlusion of the coronary ostia was found at necropsy.

Four patients (Group A), although decompensated, presented no clinical evidence of peripheral circulatory failure. The vital capacity ranged from 450 to 1,470 c.c. per square meter, with an average of 950 c.c., which is 60 per cent less than normal; the pulmonary circulation time varied between 14 and 27 seconds, with an average of 21 seconds, or 98 per cent greater than normal; while the average arm venous circulation time of 5.8 seconds (3 to 8 seconds) and the venous pressure of 9 cm. of water (8 to 11 cm.) showed relatively slight increases of 29 and 23 per cent, respectively.

The five patients of Group B were more severely decompensated and showed generalized circulatory failure. The average vital capacity, which was 1,240 c.c. per square meter (1,000 to 1,455 c.c.), was 48 per cent lower than normal; the pulmonary circulation time, 30.2 seconds (22 to 43 seconds), 185 per cent longer than the normal time; the venous circulation time, 9 seconds (6 to 13 seconds), 100 per cent longer than the normal time; and the venous pressure, 16.6 cm. of water (6 to 27 cm.), 127 per cent above the average normal pressure. In Case 7, with advanced myocardial insufficiency, the absence of clinical improvement following rest, digitalization and dehydration corresponded with the absence of significant circulatory change.

Rheumatic Heart Disease.—The nine patients (Table V) who suffered from rheumatic valvular heart disease with circulatory failure exhibited the clinical and roentgenological signs of mitral disease. Aortic valvular disease coexisted in one instance (Case 3), functional tricuspid insufficiency in two instances (Cases 3 and 4), and cardiac arrhythmia in three. In the two patients (Cases 5 and 7) who suffered from recurrent paroxysmal cardiac dyspnea and pain, severe coronary arterial disease complicated the rheumatic heart disease. Case 1 (Group A), although decompensated, showed no peripheral failure. The venous pressure of 6 cm. of water and the venous circulation time of 5 seconds are essentially normal, and are in striking contrast to the vital capacity of 1,280 c.c. per square meter, which was 46 per cent below normal, and to the pulmonary circulation time of 19 seconds, which was 79 per cent above normal.

In the eight cases (Group B) with failure of both pulmonary and peripheral circulations, the vital capacity, which averaged 1,050 c.c. per square meter (510 to 1,510 c.c.), was 56 per cent less than normal; the

TABLE V

THE PULMONARY AND PERIPHERAL VENOUS CIRCULATION TIMES IN RHEUMATIC HEART DISEASE WITH CIRCULATORY FAILURE

CASE NO.	AGE	DATE	HEART RATE	ARTERIAL PRESSURE		VENOUS PRESSURE	VITAL CAPACITY		DYE CIRCULATION TIME ARM TO FEMORAL	CYANIDE CIRCULATION TIME			REMARKS
				SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER		ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	YEARS		PER MIN.	MM. HG	MM. HG	CM. H_2O	C.C.	C.C.	SEC.	SEC.	SEC.	SEC.	
Group A. Patients with failure of the pulmonary circulation and normal peripheral circulation													
1	42	10/29/31	92	125	75	6	2700	1280	–	24	19	5	Mitral stenosis and regurgitation. Moderate failure. Orthopnea 20°. Edema 0.
Group B. Patients with failure of both pulmonary and peripheral circulations													
2	50	6/15/32	132	128	90	18	1950	1030	–	39	21	18	Mitral stenosis and regurgitation. Auricular flutter. Moderate failure. Orthopnea 30°. Edema 1+.
3	13	9/ 6/31	112	135	60	25	1350	980	–	30	23	7	Mitral and aortic stenosis and regurgitation. Tricuspid regurgitation. Advanced failure. Orthopnea 0°. Edema 4+.
		9/23/31	104	110	45	11	1550	1150	–	18	14	4	Marked improvement. Edema 0.
4	14	9/13/31	104	120	95	20	1800	1230	–	30	24	6	Mitral stenosis and regurgitation. Auricular fibrillation. Tricuspid regurgitation. Advanced failure. Orthopnea 0°. Edema 4+.
5	50	11/10/32	84	115	80	10	2200	1050	26	26	24	2	Mitral stenosis and regurgitation. Coronary disease. Orthopnea 30°. Edema 2+.
		11/30/32	60	110	65	5	4150	1980	24	28	22	6	Improved. Ambulatory. Orthopnea 10°. Edema 0.

TABLE V—CONT'D

CASE NO.	AGE	DATE	HEART RATE	ARTERIAL PRESSURE		VENOUS PRESSURE	VITAL CAPACITY		DYE CIRCULATION TIME ARM TO FEMORAL	CYANIDE CIRCULATION TIME			REMARKS
				SYSTOLIC	DIASTOLIC		OBSERVED	PER SQUARE METER		ARM TO CAROTID	CRUDE PULMONARY	VENOUS	
	YEARS		PER MIN.	MM. HG	MM. HG	CM. H_2O	C.C.	C.C.	SEC.	SEC.	SEC.	SEC.	
6	53	3/30/31	100	130	80	14	1400	510	–	42	24	18	Mitral stenosis and regurgitation. Auricular fibrillation. Moderate failure. Orthopnea 20°. Edema 2 +.
7	57	10/ 5/31	100	110	85	25	1300	830	32	36	30	6	Mitral stenosis and regurgitation. Coronary disease. Advanced failure. Orthopnea 45°. Edema 1 +.
		10/13/31	88	115	75	6	2150	1370	18	19	17	2	Improved. Orthopnea 20°. Edema 0.
8	26	12/ 1/31	104	125	95	22	1900	1270	–	55	35	20	Mitral stenosis and regurgitation. Advanced failure. Orthopnea 35°. Edema 4 +. Died 2 months later.
9	30	2/27/32	132	135	80	19	2560	1510	24	25	–	–	Mitral stenosis and regurgitation. Regular rhythm. Advanced failure. Orthopnea 40°. Edema 4 +. Died suddenly 24 hours later.

pulmonary circulation time, averaging 25.9 seconds (21 to 35 seconds), and the venous circulation time, averaging 11 seconds (2 to 20 seconds), were both 144 per cent greater than normal; and the venous pressure, averaging 19.1 cm. of water (10 to 25 cm.), was 162 per cent above normal. Coincident with clinical improvement in three patients (Cases 3, 5 and 7) there was an increase in the average vital capacity from 953 to 1,500 c.c. per square meter; a decrease in the pulmonary circulation from 25.7 to 17.7 seconds and in the venous circulation time from 5 to 4 seconds; and a decrease in the venous pressure from 20 to 7.1 cm. of water.

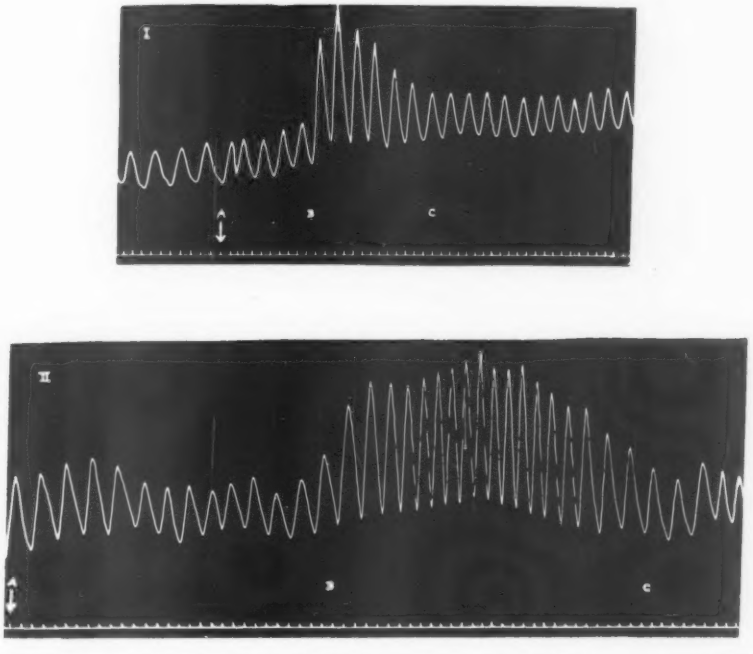

Fig. 1.—Comparison of the respiratory response to cyanide in a normal subject (tracing 1) and in a patient with congestive failure (tracing 2). *A*, Injection; *B*, onset of respiratory stimulation (10 and 29 sec., respectively); *C*, return to normal respiration (24 and 60 sec., respectively). Note the more delayed intense and prolonged stimulation of respiration in the patient with congestive failure.

The Dosage of Cyanide and Respiratory Response in Circulatory Failure

The reaction to cyanide in patients with cardiac decompensation differs in several respects from the reaction in normal subjects. Smaller doses of cyanide as a rule cause adequate respiratory stimulation. The average optimal dose for antecubital injection, 5.2 mg., or 0.26 c.c. of 2 per cent aqueous solution, or 0.084 mg. per kilogram, was approximately 25 per cent smaller than the average normal dose. As in normal subjects, approximately two-thirds of the antecubital dose gave a comparable response from jugular injection. In view of the increase in dosage found necessary with the radium emanation[11] and histamine[3]

methods as a result of "stringing out" in the blood stream, this reduction in dosage is particularly significant and may indicate a lowering of the threshold for cyanide stimulation during circulatory failure. In our experience no untoward results have followed the administration of sodium cyanide to patients with circulatory failure except in one subject with malignant hypertension and nausea, in whom vomiting occurred.

The respiratory response to cyanide in circulatory failure is characterized by a relatively gradual onset, a more moderate increase in the rate and the amplitude of respiration, and a more gradual return to natural breathing. In severe failure, the response may extend over a period several times as long as that occupied by the transient type of reaction

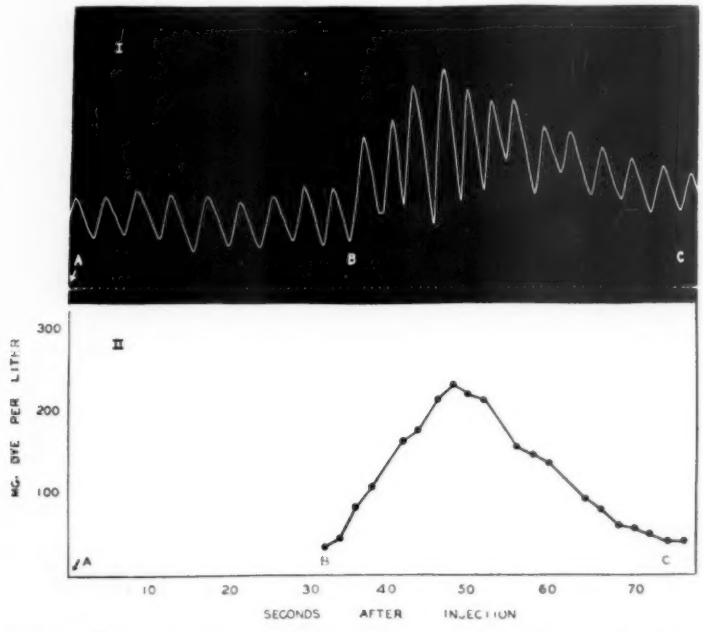

Fig. 2.—Comparison of the respiratory response to cyanide (tracing 1) with the dye distribution curve (tracing 2) in the same patient with heart disease. *A*, Time of injection; *B*, onset of respiratory stimulation (34 sec.), and appearance of dye in the femoral artery (32 sec.); *C*, disappearance of respiratory stimulation (74 sec.) and of the dye (74 sec.). Note the similarity of the two curves.

observed in normal subjects. Normal and pathological types of respiratory response are illustrated by the tracings in Fig. 1.

The long continued stimulation of respiration by cyanide in circulatory failure is indirect evidence of the "stringing out" of the blood stream during its passage through the heart and lungs, which was postulated by Blumgart and Weiss[11] and other investigators, and has recently been demonstrated by the flattening and prolongation of the vital red distribution curve.[12] The general similarity between the respiratory response to cyanide and the dye distribution curve in patients with circulatory failure (Fig. 2) suggested the employment of cyanide

for the estimation of the "mean pulmonary circulation time." While this measurement was not feasible with the cyanide method, the character of the curve reflects the character of blood flow through the lungs.

DISCUSSION

Critique of Method

The reliability of the cyanide method for measurements of the velocity of blood flow depends primarily upon the accuracy with which the arrival of the cyanide in the carotid sinus is registered by respiratory stimulation. In circulatory failure, the accumulation of blood in the pulmonary circuit and the different velocities of blood flow through the vascular areas of the lungs cause a lowering of the initial concentration of cyanide arriving in the carotid sinus, and this tends to obscure or delay the onset of the respiratory response. The hyperirritability of the respiratory center under these circumstances, however, counteracts this tendency and thus lessens or prevents erroneous prolongation of the circulation time. In order to evaluate the reliability of the cyanide method, the results obtained were compared with those obtained with the radium emanation and dye methods.

Comparison With the Radium Emanation Method.—In patients with heart disease, as in normal subjects, the results obtained with the cyanide and radium emanation methods were found to be almost identical.[7] In patients with compensated cardiovascular disease the velocity of pulmonary blood flow as measured by both methods was found to be normal or slightly diminished, and the peripheral circulation essentially normal (Table I). In the forty-six patients with circulatory failure, on the other hand (Tables II to V), the cyanide pulmonary circulation time averaged 23.2 seconds (13 to 45 seconds), or 119 per cent longer than the normal time; while the pulmonary circulation time measured by the radium emanation method in twenty-two patients with comparable types of heart disease and comparable severity of failure averaged 26.1 seconds (14.5 to 67 seconds), or 142 per cent longer. The general correspondence of the severity of decompensation in these two groups of patients is further indicated by the reduction of the vital capacity to 1,071 and 1,349 c.c. per square meter, respectively. Measurements of the velocity of venous blood flow were also in satisfactory although less striking agreement. The average cyanide arm venous circulation time, or "venous velocity index," was 7.5 seconds (2 to 25 seconds), or 67 per cent longer than the normal time, as compared with the "arm to heart" circulation time of the radium emanation method of 14.5 seconds (4 to 31 seconds), which was an increase of 123 per cent. The shorter circulation times of the pulmonary and peripheral venous circulations obtained with the cyanide method indicate the reliability of the method.

Comparison With the Dye Circulation Time.—In normal subjects, the cyanide arm-to-carotid circulation time is in close agreement with the arm-to-femoral circulation time determined by the dye or glucose method; in eight subjects it was found to average 1.3 seconds less than the glucose circulation time.[7] Forty determinations made with these methods in twenty-seven patients with circulatory failure revealed in general a satisfactory agreement (Tables II to V): 26.7 seconds (15 to 65 seconds) for the average cyanide circulation time; and 25.1 seconds (15 to 68 seconds) for the dye circulation time. In twenty-five determinations (with one exception) the cyanide circulation time was the greater by 1 to 6 seconds; in eight determinations it was the smaller by 1 to 4 seconds; and in seven instances no difference was detected. The more uniform concordance observed in normal subjects is not to be expected here, as the comparative determinations were made consecutively, not simultaneously, and were carried out under the slightly different experimental conditions required by each method. Case 9 (Table IV) illustrates the accuracy of the cyanide circulation time in extreme circulatory failure marked by intense dyspnea and pronounced retardation of blood flow. The cyanide circulation time was prolonged to 65 seconds; the dye circulation time measured 68 seconds.

The close correspondence of the measurements of the pulmonary circulation time obtained with the cyanide, radium and dye methods is substantial evidence that in patients with cardiovascular disease, as in normal subjects, the cyanide method provides a practical and reliable index of the velocity of pulmonary and peripheral venous blood flow.

Types of Circulatory Failure and Changes in the Hemodynamics

A correlation of the results of the circulatory measurements with the degree of disability of the patients failed to reveal a strict relationship. In general, the greater the deviation from the normal values, the more severe were the symptoms. The reverse relationship, namely, marked cardiac disability associated with great changes in the blood flow and in other aspects of the circulation, was not necessarily present.

Among the aspects of the circulation studied, the vital capacity of the lungs was the first to show a change. At times it reached a level of 50 per cent of the normal value, while the pulmonary blood flow showed only a slight degree of slowing. With more severe circulatory failure further reduction in the vital capacity of the lungs was relatively small, while the slowing of the pulmonary blood flow became rather marked. At this stage there often appeared also a decrease in the velocity of the venous blood flow and a progressive elevation of the peripheral venous pressure. These findings suggest that a relatively small amount of pulmonary engorgement can induce an appreciable reduction in the vital capacity of the lungs, while further engorgement produces proportionately little change.

We wish to call particular attention to the behavior of the circulation in two groups:

1. In several instances (Cases 1, 3, 10—Table II; Case 1—Table IV) the pulmonary circulation time remained within normal limits despite clinical, x-ray and vital capacity findings characteristic of pronounced stasis in the pulmonary circulation. The exact explanation of these findings cannot be given from available data, but there is evidence suggesting that pulmonary vascular hypertension was the responsible factor. The sharply accentuated, ringing, pulmonic second sound invariably present speaks also for exceptional pulmonary hypertension in these cases, while the values for cardiac output, pulmonary blood volume, minimal and mean pulmonary circulation time obtained with the vital red method[10] denote the relative normality of blood flow through the lungs, and therefore exclude pulmonary stasis as an important factor.[13] The inference is that the manifestations of circulatory failure, under these circumstances at least, are caused primarily by an increased pressure in the pulmonary vascular bed which induces stiffening of the lungs and extravasation of fluid from the pulmonary capillaries, without alteration of the pulmonary blood flow.

2. In a group of patients with arterial hypertension, and with syphilitic and arteriosclerotic heart disease often associated with cardiac asthma and marked disability, there occurred a reduction in the vital capacity of the lungs and a slowing of the pulmonary blood flow, but no retardation of the peripheral venous blood flow and no elevation of the venous pressure. This behavior of the peripheral blood flow was verified clinically by the rapid filling of the brachial vein following emptying, and by the absence of peripheral edema and hepatic enlargement. In several instances the venous circulation time was appreciably shortened. This latter behavior of the venous circulation may be the result of the following factors singly or combined: (a) a constriction of the peripheral veins, as observed in a number of these patients; (b) an increase in the aspiratory action of the thorax, as indicated by the inspiratory retraction of the intercostal spaces, and by the simultaneous rhythmic fall in the arterial and venous pressures; (c) an accumulation of blood in the lungs, leading to a reduction of the peripheral circulatory blood volume.

These clinical and experimental observations indicate that *failure of the pulmonary circulation alone is frequently responsible for severe disability.* In the majority of instances of circulatory failure, however, severe disturbance of the pulmonary circulation is associated with changes in the greater circulation.

SUMMARY

1. Sodium cyanide in amounts sufficient to produce adequate stimulation of respiration can safely be administered to patients with cardio-

vascular disease. The average effective dosage is approximately three-fourths that required by normal subjects: 5.2 mg., or 2.6 c.c. of a 2 per cent solution, which is equivalent to 0.084 mg. per kilogram. The fact that the respiratory center is hyperirritable to cyanide in the presence of circulatory failure makes this method particularly suitable for the measurement of the velocity of blood flow in heart disease. No untoward results have followed its administration to patients with circulatory failure when given in amounts sufficient to produce marked stimulation of respiration.

2. The curve representing respiratory response following administration of cyanide reveals the character of the pulmonary blood flow in heart disease.

3. Comparative measurements of the circulation time obtained with the cyanide, radium emanation, and vital red methods reveal that results obtained with the cyanide method are reliable indices of the velocity of blood flow in the pulmonary and peripheral venous circulations. As a rule the prolongation of the circulation time paralleled the severity of circulatory failure.

4. Marked reduction in the vital capacity of the lungs may develop at an early stage of circulatory failure when the velocity of pulmonary blood flow shows slight or no decrease and the peripheral venous circulation, as well as the venous pressure, is normal.

5. In a group of patients with arterial hypertension and intense dyspnea, evidence was obtained that pulmonary vascular hypertension existed without retardation of the blood flow through the lungs.

6. In a group of patients with disability due to hypertensive, syphilitic, or arteriosclerotic cardiovascular disease, disturbances of the pulmonary circulation were associated with normal peripheral venous circulation.

7. Owing to the numerous factors influencing hemodynamics, no strict correlation existed between clinical manifestations and the aspects of the circulation studied. Statistically, progressive reduction in the vital capacity and in the velocity of the pulmonary and peripheral venous blood flow, as well as an elevation of the venous pressure, are associated with an increasing degree of disability.

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PULMONARY HEART DISEASE IN PNEUMOCONIOSIS*

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PULMONARY heart disease, or *cor pulmonale,* is an entity characterized by right ventricular enlargement, especially marked in the outflow tract (conus arteriosus and pulmonary artery). It results from diseases which impede the pulmonary circulation, and has been recognized at post-mortem examinations for a great many years. Schroetter[1] described it in 1876. Similarly it is referred to in most textbooks of pathology (e. g., MacCallum[2]) and in exhaustive treatises on heart disease (e. g., White[3]) where it receives adequate description of its etiology, symptomatology, diagnosis, and treatment.

The ante-mortem diagnosis of pulmonary heart disease could not be proved before the advent of the roentgen-ray and the electrocardiogram. With progress in roentgen-ray study of heart disease, however, right ventricular enlargement is now recognizable when the normal concavity on the left border of the cardiac silhouette is replaced by a bulging convexity representing enlargement of the pulmonary artery and conus arteriosus. This fundamental observation was first made by Assmann,[4] and has been emphasized repeatedly since.[5, 6, 3, 7, 8, 9, 10, 11] Electrocardiography further enhances the possibility of diagnosis when showing right axis deviation.

The present paper is concerned with pulmonary heart disease resulting from pneumoconiosis in anthracite coal miners—a group which inhales great amounts of carbon together with silica particles, is not particularly susceptible to tuberculosis, and achieves fair average longevity. The conclusions reached are believed applicable in this type of pneumoconiosis, but by no means should they be applied to the pure silicosis of noncarbon workers, a disease generally terminating *early* in disability and death from "silico-tuberculosis."

Because of its industrial incidence, disabling features, and compensation potentialities, pneumoconiosis has achieved great importance. As a disease entity characterized by long-standing pulmonary fibrosis, sufficient to impede pulmonary circulation, it is urged that it be entitled to a place of its own among the potential causes of pulmonary heart disease. Furthermore, since the roentgen-ray and electrocardiogram together are now able to indicate the presence of pulmonary heart disease ante-mortem, it seems expedient to present our observations regarding its incidence and symptomatology in a series of anthracite coal miners.

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While *cor pulmonale* has an incidence of only 0.9 per cent in Boston, as White[3] states, it is not so infrequent in the hard coal regions, and should not be neglected as an oddity. Future investigations of pneumoconiosis will be far more accurate in prognosticating disability from right heart failure if the pulmonary artery shadow is understood, and if the presence or absence of right axis deviation is ascertained with the galvanometer. (If pneumoconiosis eventually becomes compensative, the economic aspect of these facts may be enormously important.)

INCIDENCE

From July, 1931, to October, 1933, 213 cases of pneumoconiosis were examined in the Hazleton State Hospital. Of these 51 (or 24 per cent) were first stage, 94 (or 44 per cent) were second stage, and 56 (or 26 per cent) were third stage cases. The classification is that of Pancoast and Pendergrass, as given by Sante.[12] Twelve cases (or 6 per cent) were unclassified since the pathologic condition was doubtful, or the probability of tuberculosis great.

In 86 patients the pneumoconiosis was probably insufficient materially to increase the resistance to the pulmonary circulation. These were generally the first or early second stage cases. In 127 patients the pneumoconiosis was marked enough to obstruct the pulmonary circulation. These were the marked second and third stage cases. Table I shows the

TABLE I

INCIDENCE

TYPE OF CARDIAC SILHOUETTE	SUFFICIENCY OF PNEUMOCONIOSIS TO RESIST PULMONARY CIRCULATION	
	INSUFFICIENT 86 CASES	SUFFICIENT 127 CASES
Normal cardiac silhouettes	64	81
Enlargement of transverse diameter (unrelated cardiac hypertrophy)	14	17
Tortuosity, dilatation, of aorta (arteriosclerotic heart disease)	5	11
Enlargement of pulmonary artery and conus shadows (pulmonary heart disease)	0	18
Same, but from mitral stenosis	3	0
Totals	86	127
Total cases of pneumoconiosis studied: 213		

various types of cardiac silhouettes found, together with their incidences.

Pulmonary heart disease, evidenced by enlargement of the pulmonary artery and conus shadows, was found in 18 cases. The incidence, therefore was 14 per cent (18 among 127 cases) in pneumoconiosis sufficient to cause it, and 8.4 per cent (18 among 213 cases) in pneumoconiosis of all stages. Incidence based on the total number of cases of all organic heart disease (miners and non-miners) seen in the hospital during the same period is 2.9 per cent (18 among 608 cases).

TABLE II

SYMPTOMATOLOGY

CASE	AGE	YEARS AS MINER		PULMONARY SYMPTOMS (COUGH, EXPECTORATION, ASTHMA)	CARDIAC OR PULMONARY SYMPTOMS (DYSPNEA, CYANOSIS, CONGESTION)	X-RAY FINDINGS			ELECTROCARDIOGRAM	REMARKS; PRESENT CONDITION
		COAL DUST	ROCK DUST			STAGE PNEUMOCONIOSIS	PROMINENT PULMONARY ARTERY	ENLARGED HEART RIGHT TO RIGHT LEFT TO LEFT		
1. M. H.	67	20+	4+	+	++	2	yes	no	R.A.D.	Died, autopsy
2. J. K.	49	27	5	++	+	2	yes	no	R.A.D.	TB ?
3. A. G.	51	30	?	+	0	3	yes	no	none made	Died, no autopsy
4. M. F.	52	10	1+	+	+	3	yes	R	R.A.D.	Disabled
5. J. G.	45	26	7	+	0	3	yes	no	R.A.D.	Disabled
6. H. C.	43	17	6	+	+	3	yes	no	R.A.D.	Disabled
7. S. C.	39	22	?	+	0	2	yes	no	R.A.D.	Working
8. J. S.	38	20	10	+	sl.	2	yes	R & L	R.A.D. Prom. P waves	Working
9. C. A.	35	17	½	+	++	2	yes	R & L	R.A.D. T_2 change	Working
10. J. B.	57	37	0?	+	+	3	yes	no	L.A.D. $T_{1,2}$ change	Disabled, sclerosis
11. W. D.	39	16	½	+ sl.	+	1	yes	no	R.A.D.	?
12. I. K.	64	40	2-3	+	sl.	3	yes	no	R.A.D. Aur. fibrillation	Disabled
13. J. R.	37	21	3	+	+	2	yes	no	R.A.D. Extrasystoles	?
14. P. P.	38	16	1+	+ ?	+	2	yes	R & L	Normal	?
15. M. C.	24	4	2	0	0	2	yes	no	R.A.D.	Working
16. J. M.	52	23	1	+	+	2	yes	no	R.A.D. Prom. P waves	Disabled
17. M. M.	39	5	?	+	++	2	yes	R	R.A.D. $T_{2,3}$ change. Aur. Fibrillation	Disabled
18. J. R.	45	20	1-2	+	++	2	yes	no	Tendency to R.A.D. $T_{2,3}$ change	?

SYMPTOMATOLOGY

In this series of 18 cases, none had histories of syphilis, and none had positive or doubtful Kahn tests. None presented a history of rheumatic fever except Case 18 (J. R.). No case presented clinical evidence of

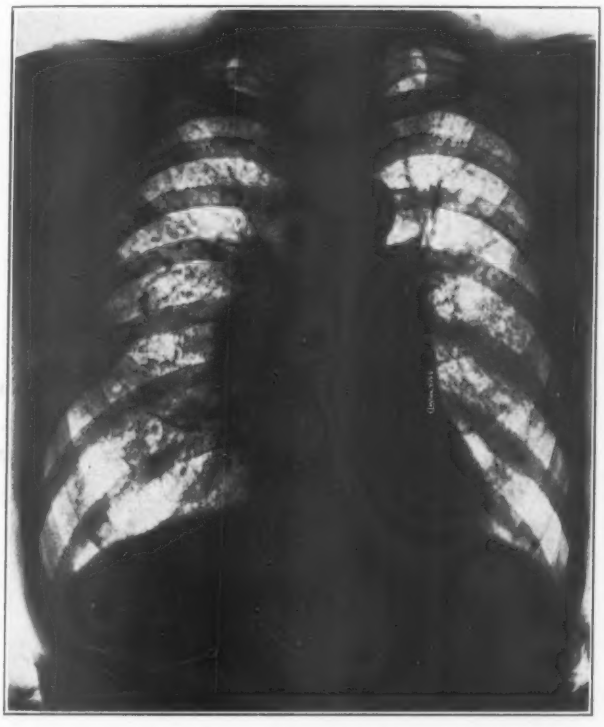

Fig. 1.—Case 1, M. H., second stage pneumoconiosis, with pulmonary heart disease, confirmed by autopsy.

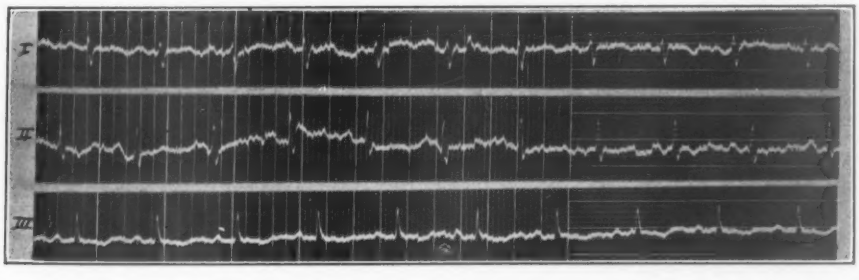

Fig. 2.—Electrocardiogram of Case 1, made two hours before death; right axis deviation.

mitral stenosis. All blood pressure readings were considered normal or subnormal for the age. Many of the cases showed a pulmonic second sound louder than the aortic. The important symptoms together with the roentgenological and electrocardiographic findings are tabulated in Table II.

The chest films, together with the electrocardiograms of 2 cases are illustrated. (Figs. 1, 2, 3, 4.) Cases 2, 3, 4, 5, and 6 were illustrated in a previous publication.[11] The remainder of the series have similar chest

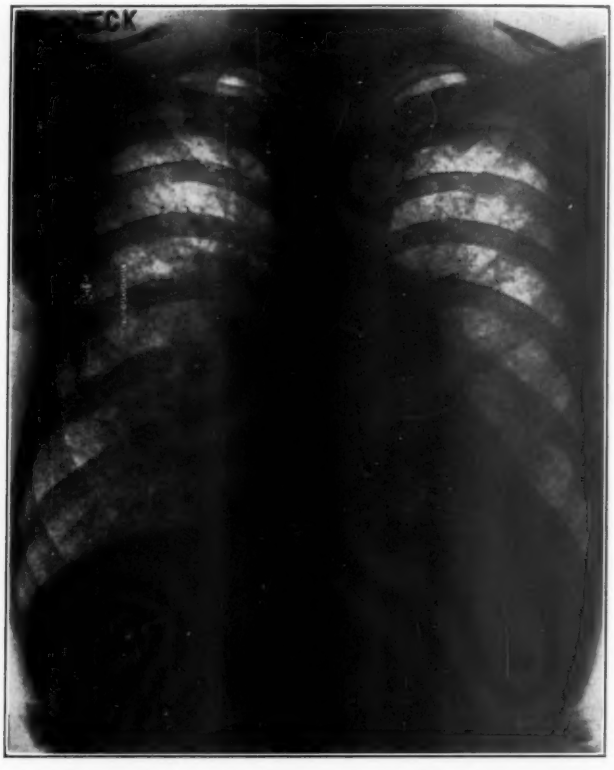

Fig. 3.—Case 8, J. S, second stage pneumoconiosis, with enlargement of transverse diameter of the heart to right and left, and pulmonary heart disease.

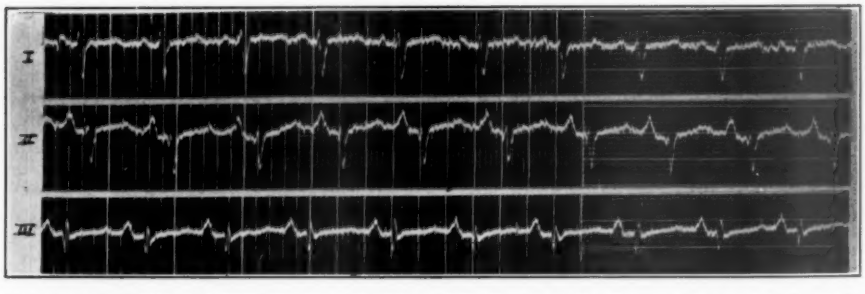

Fig. 4.—Electrocardiogram of Case 8. Right axis deviation; prominent P-waves in Leads II and III.

films. The electrocardiograms also are similar to those illustrated, with the exception of Cases 10, 14, and 18, which showed left axis deviation, normal tracing, and "tendency to right axis deviation" respectively.

Case 13 presented frequent extrasystoles. Cases 12 and 17 showed auricular fibrillation together with right axis deviation. T_1 or T_2 inversion was met with in Cases 9, 10, 17, and 18. Abnormally large P-waves were found in Cases 8 and 16. Attention is called to the fact that, while the majority of these patients are disabled, only two are known to have died.

Post-mortem examination was obtained on Case 1, M. H., who died of right heart failure. The heart weighed 450 grams. The pulmonary artery was much larger than the aorta and was greatly distended. The right chambers were enlarged. All valves were of normal structure, and their circumferences in centimeters were: aortic 9.0, pulmonic 11.5, mitral 8.7, and tricuspid 11.0. The thickness of the right ventricular wall varied between 0.7 and 1.3 cm. near the apex to 2.0 cm. at the base near the tricuspid valve. The thickness of the left ventricle did not exceed 1.9 cm. (Microscopic study showed hyperplasia and hypertrophy in the right ventricular myocardium. Pale staining was noted, and also hydropic degeneration and degenerative fragmentation.)

SUMMARY AND CONCLUSIONS

1. Pulmonary heart disease is described, together with its diagnosis by roentgenography and electrocardiography.

2. A series of 18 cases of its occurrence in pneumoconiosis is presented to illustrate incidence and symptomatology.

3. The disability and incidence indicate that pulmonary heart disease is not a rarity in anthracite coal miners, and must not be neglected.

4. It is urged that pneumoconiosis, because of its great economic and industrial importance, be more generally considered an important cause of pulmonary heart disease.

5. No attempt is made to explain why pulmonary heart disease occurs in some cases of marked pneumoconiosis, but not in others equally marked.

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THE EFFECT OF GENERALIZED ANOXEMIA ON THE ELECTROCARDIOGRAM OF NORMAL SUBJECTS. ITS BEARING ON THE MECHANISM OF ATTACKS OF ANGINA PECTORIS*†

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EVIDENCE has accumulated that characteristic changes in the S-T segment and T-wave accompany spontaneous and induced attacks of angina pectoris.[1-9] The procedures (viz., exercise, insulin, adrenalin, generalized anoxemia, etc.) employed to bring on attacks of angina pectoris in patients suffering from this disease have been found to produce the electrocardiographic changes even when they failed to cause anginal attacks.[6-9] Furthermore these procedures have been found to cause similar electrocardiographic changes in patients without a history of angina pectoris and in normal subjects used as controls (Katz, Hamburger and Lev,[6] Scherf and Goldhammer,[8] and Rothschild and Kissin[9]). The number of normal subjects so studied has been limited. The present report deals with observations on a further group of seventeen normal subjects. It supports the view that electrocardiographic changes such as occur during anginal attacks can appear without being accompanied by angina pectoris.

Generalized anoxemia such as that produced in the present study, has been reported to cause shifts in the S-T segment in animals (Kountz and Gruber[10] and more recently Kountz and Hammouda[11]). Greene and Gilbert[12] reported that the T-wave in normal human subjects became flattened, diphasic or inverted as anoxemia developed. However, they did not report on the effect of anoxemia on the S-T segment. Recently, Rothschild and Kissin[9] found a depression in the S-T segment in one of the two normal subjects they studied, and no change in the other.

METHOD

The generalized anoxemia was induced by rebreathing from a recording segment spirometer of 70 liter capacity similar to the one designed by Burlage and Wiggers;[13] a two-way flap valve was used to direct the expired air back into the spirometer through a soda-lime container to remove the CO_2. The completeness of CO_2 removal was checked by analyzing samples of air from the spirometer with Marriott tubes.[14] Before each experiment the spirometer was thoroughly aerated and then calibrated. The subject reclined comfortably on a cot during the rebreathing. Con-

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trol electrocardiogram, blood pressure and heart rate were obtained, and these observations were repeated during the course of the anoxemia and following the resumption of breathing room air. The respiratory excursions were inscribed on a smoked paper kymograph by means of a lever moving with the rubber covered top of the segment spirometer. The excursion was calibrated in liters, and time was recorded in 5-second intervals. The minute volume of respiration was obtained from the curve by computing the product of amplitude of respiration in liters and the rate of respiration per minute; the control reading was obtained from the curve inscribed during the first minute of rebreathing. Since the expired CO_2 was absorbed before the rebreathed air was returned to the spirometer, there is a slight error in this computation.

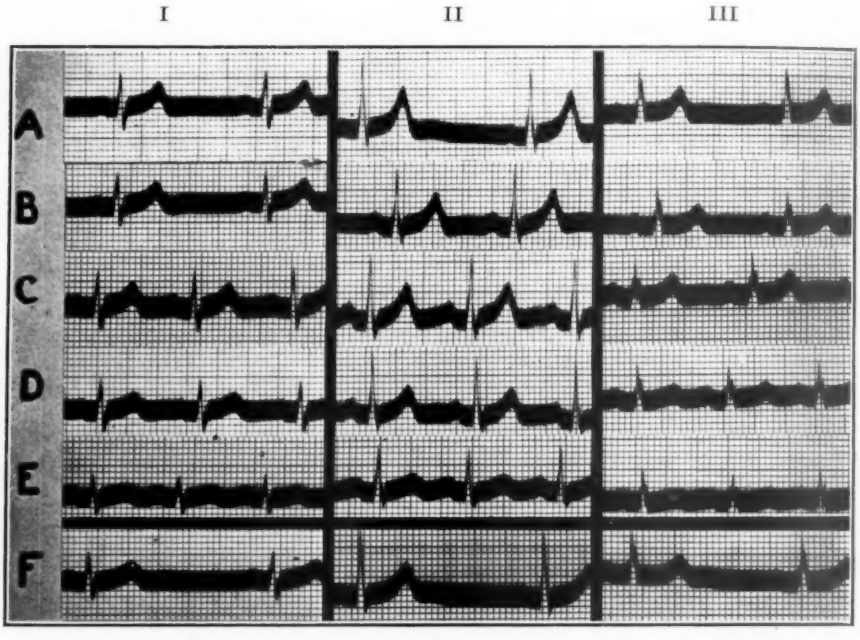

Fig. 1.—Normal subject W.S. Standard three leads of electrocardiogram during induced generalized anoxemia. Segment A, control while breathing room air. Segments B, C, D and E successive stages during rebreathing (D and E being taken in rapid succession just before end), O_2 content of inspired air being respectively about 17.8, 13.7 and 9.6 volumes per cent. Segment F was taken two minutes after resuming breathing of room air.

The level of the pointer moving with the rubber covered top of the segment spirometer was maintained constant by running in water throughout the experiment from a graduated 20 liter bottle in amounts sufficient to replace the oxygen consumed. The oxygen content at various stages of the test was computed from the quantity of water run out of the bottle at the time of estimation. As a check, a sample of the spirometer air obtained at the end of the rebreathing was analyzed with a Haldane apparatus for its O_2 and CO_2 content.

The rebreathing was terminated on signal whenever the subject felt moderately uncomfortable. However, the subject was closely watched, since events move rapidly at the critical stage and unconsciousness may develop abruptly. The duration of the rebreathing period in this series varied from twenty-five to thirty-five minutes.

RESULTS

The essential changes observed in this series of subjects are summarized in Table I, and records illustrative of the sequence of the electrocardiographic alterations are shown in Figs. 1 to 4.

It was found that during the induced generalized anoxemia, the most consistent changes in the electrocardiogram were a flattening of the T-

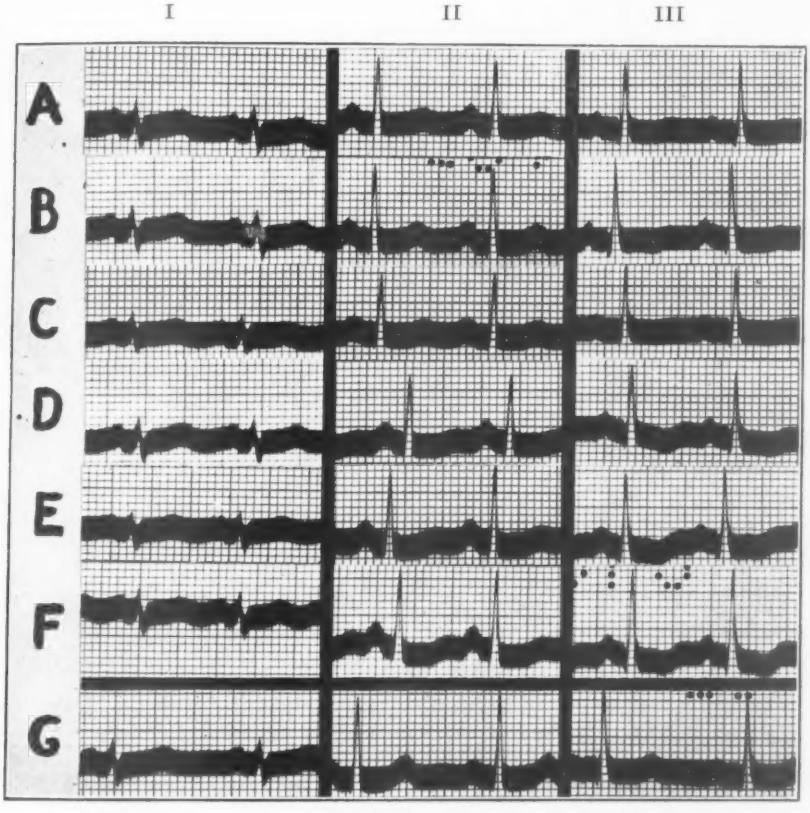

Fig. 2.—Normal subject C.M. Standard three leads of electrocardiogram during induced generalized anoxemia. Segment A, control while breathing room air. Segments B, C, D, E and F, successive stages during rebreathing (E and F being taken in rapid succession just before end), O_2 content of inspired air being respectively about 18.4, 15.8, 13.2 and 10.6 volumes per cent. Segment G was taken seven minutes after resuming breathing of room air.

wave in one or more leads, in some instances followed by its inversion (Figs. 2 and 4). In practically every instance, the level of the S-T segment tended to be shifted downward during anoxemia. Since the S-T segment in many of these subjects was definitely elevated above the isoelectric level at the start—a not uncommon finding in normal individuals—the downward shift during anoxemia resulted, in some instances, merely in the S-T segment becoming less elevated. However,

TABLE I

NORMAL SUBJECTS

SUBJECT	INSPIRED O_2 AT END OF TEST (VOL. %)	BLOOD PRESSURE (MM. HG)			HEART RATE (PER MIN.)			RESPIRATORY RATE (PER MIN.)		RESPIRATORY VOLUME (L. PER MIN.)		CHANGES IN P-R INTERVAL	CHANGES IN QRS AMPLITUDE	CHANGE IN LEVEL OF S-T INTERVAL			CHANGE IN AMPLITUDE OF T-WAVE MM.		
		CONTROL	END OF TEST	5 MIN. LATER	CONTROL	END OF TEST	5 MIN. LATER	CONTROL	END OF TEST	CONTROL	END OF TEST	LEAD II		LEAD I	LEAD II	LEAD III	LEAD I	LEAD II	LEAD III
J.P.	13.5				75	91	72	10	10	10	16	0.16 to 0.16	smaller all leads**	++ to +	+ to 0	0 to 0	+2 to +1	+1 to $-\frac{1}{2}+\frac{1}{2}$	-1 to $-\frac{1}{2}$
R.S.	8.7				96	111	91	9	18	13	22	0.12 to 0.14	smaller Leads II and III	0 to 0	0 to 0	0 to 0	$+1\frac{1}{2}$ to +1	+2 to $+1\frac{1}{2}$	+1 to $+\frac{1}{2}$
H.G.	9.5				86	107	83	20	19	10	23.5	0.18 to 0.20	no change	+ to 0	0 to 0	0 to 0	+2 to +1	$+2\frac{1}{2}$ to +1	$+\frac{1}{2}$ to ± 0
D.K.	11.3				75	94	72	17	19	8.5	19	0.16 to 0.18	smaller all leads	+ to 0	+ to 0	0 to −	$+1\frac{1}{2}$ to +1	$+2\frac{1}{2}$ to $+1\frac{1}{2}$	+1 to +1
W.S.	9.6				60	103	56	19	25	13	22	0.14 to 0.18	smaller all leads	+ to 0	+ to 0	+ to 0	+3 to +1	+6 to $+1\frac{1}{2}$	+3 to $+\frac{1}{2}$
J.R.*	8.5				79	130	70	15	18	7.5	11	0.14 to 0.14	smaller all leads	0 to −	+ to −	0 to −	+1 to $+\frac{1}{2}$	+1 to ± 0	$+\frac{1}{2}$ to -2
C.M.*	10.6				94	115	83	14	19	11	14	0.16 to 0.14	smaller all leads (slightly)	+ to 0	0 to −	0 to −	$+1\frac{1}{2}$ to +1	+1 to ± 0	$+\frac{1}{2}$ to ± 0
E.S.*	12.6	125/80	130/80	110/85	72	111	68	17	29	10.5	43.5	0.14 to 0.14	smaller all leads	0 to 0	0 to 0	0 to −	$+1\frac{1}{2}$ to $+\frac{1}{2}$	+2 to $+\frac{1}{2}$	+1 to $+\frac{1}{2}$
P.B.*	9.8	120/65	125/45		83	125	79	12	23	7	14.5	0.12 to 0.12	no change	0 to 0	0 to −	0 to −	+2 to $+\frac{1}{2}$	+3 to ± 0	+1 to ± 0
W.M.	8.5	135/80	160/55	145/80	100	125	96	13	40	10	32	0.18 to 0.18	smaller all leads	+ to −	+ to −	0 to −	$+\frac{1}{2}$ to $+\frac{1}{2}$	+4 to +1	+2 to $+\frac{1}{2}$
G.J.	7.1	120/75	165/70	120/75	60	125	60	8	27	8	27	0.14 to 0.12	smaller all leads	+ to 0	+ to −	0 to −	+2 to +1	$+2\frac{1}{2}$ to $+\frac{1}{2}$	$+\frac{1}{2}$ to ± 0
K.J.	6.6	145/85	165/80	130/80	83	143	88	7	19	11	57	0.16 to 0.16	smaller all leads	0 to −	0 to −	0 to −	$+1\frac{1}{2}$ to $+\frac{1}{2}$	$+2\frac{1}{2}$ to +1	+1 to $+\frac{1}{2}$

TABLE I—CONT'D

SUBJECT	INSPIRED O_2 AT END OF TEST (VOL. %)	BLOOD PRESSURE (MM. HG)			HEART RATE (PER MIN.)			RESPIRATORY RATE (PER MIN.)		RESPIRATORY VOLUME (L. PER MIN.)		CHANGES IN P-R INTERVAL	CHANGES IN QRS AMPLITUDE	CHANGE IN LEVEL OF S-T INTERVAL			CHANGE IN AMPLITUDE OF T-WAVE MM.		
		CONTROL	END OF TEST	5 MIN. LATER	CONTROL	END OF TEST	5 MIN. LATER	CONTROL	END OF TEST	CONTROL	END OF TEST	LEAD II		LEAD I	LEAD II	LEAD III	LEAD I	LEAD II	LEAD III
H.K.	9.9	130/ 55	125/ 40	135/ 65	73	107	66	14	17	8	15	0.20 to 0.20	smaller all leads	+ to −	0 to −	− to −	+3 to +½	+3 to +1	+1 to +½
L.R.	9.3	110/ 70	130/ 0	110/ 70	79	115	70	19	17	9.5	16	0.16 to 0.16	smaller all leads	+ to 0	+ to −	+ to 0	+2 to +1	+4 to +1½	+2 to +½
A.S.	10.1	120/ 90	125/ 80	125/ 80	83	100	70	18	18	9	18	0.16 to 0.16	smaller all leads	0 to 0	0 to 0	0 to 0	+1 to +½	+1 to +½	−½+½ to −½+½
R.L.	9.1	145/ 80	140/ 70	150/ 95				10	18	11	27								
J.L.	10.5	125/ 75	130/ 90	110/ 80				14	19	11.5	39								
PATIENTS WITH A HISTORY OF ANGINA PECTORIS																			
A.F.†	8.7	120/ 80	115/ 70	110/ 80	100	107	88	22	20	14	27	0.18 to 0.18	smaller Leads I and III††	+ to + +	+ to +	0 to 0	−1 to −½	−1 to ±0	+½ to +½
T.P.	9.0†	145/ 90	145/100	150/ 95	91	115	93	16	20	12	20	0.16 to 0.16	smaller Leads I and II larger Lead III	0 to −	0 to −	0 to 0	+½ to +½	+1 to +1½	+½ to +½
L.F.†	10.4	180/106	168/100	184/104	115	125	107	20	14	11	29	0.18 to 0.18	smaller all leads	− to − −	− to − −	− to − −	+1 to +1	+2 to +1½	+1 to +1½
W.A.	7.6	206/106	216/124	204/108	79	107	79	17	21	13	21	0.14 to 0.12	smaller all leads**	− to − −	− to − −	− to − −	−3 to −2	−2 to −3	+1 to +½
M.F.†	8.1	180/116	216/120	184/112	72	91	72	13	15	10.5	24	0.14 to 0.14	smaller all leads**	− to − −	0 to −	+ to −	+1 to +1	+2 to +1	+1 to ±0
J.F.†	13.2	160/ 80	178/ 90	160/ 80	100	107	94	18	19	7	9.5	0.16 to 0.16	smaller all leads**	− to −	− to −	+ to +	+1 to +½	+1½ to +1½	+½ to +1

*Female. **QRS_3 inverted. †Developed no pain. ††QRS_1 and $_2$ inverted.

in many instances the S-T segment actually became isoelectric or was depressed below the isoelectric level.

The changes in the T-wave and in the S-T segment were progressive in character and developed gradually as the oxygen in the inspired air

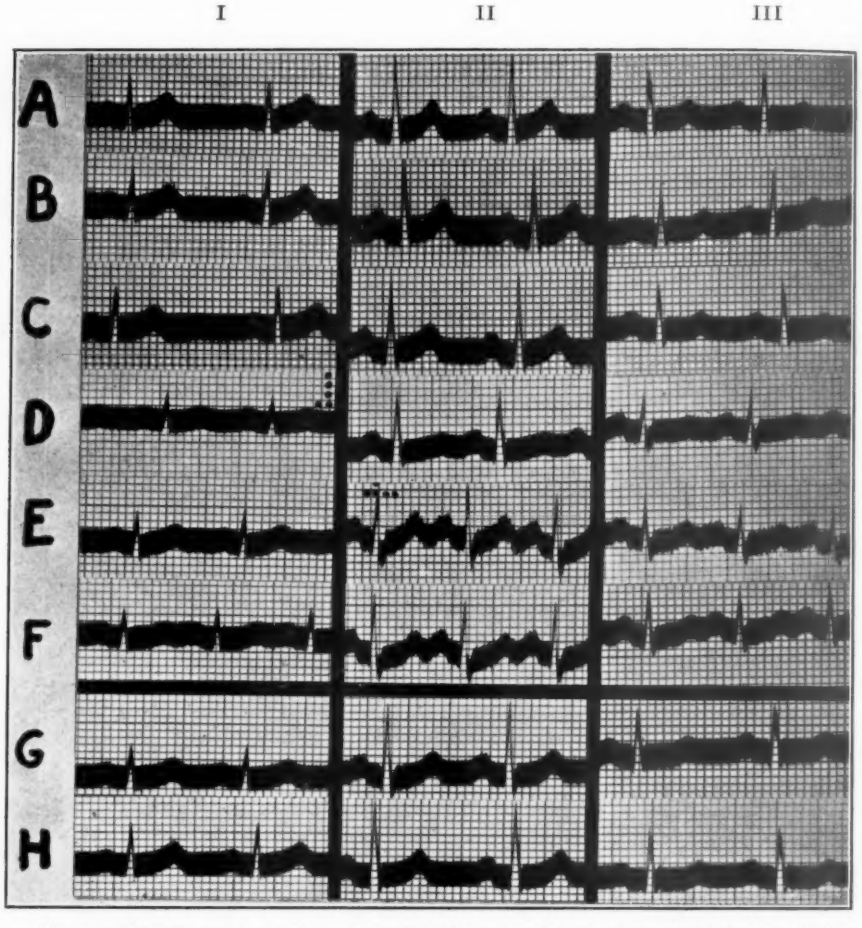

Fig. 3.—Normal subject K.J. Standard three leads of electrocardiogram during induced generalized anoxemia. Segment A, control while breathing room air. Segments B, C, D, E and F, successive stages during rebreathing (E and F being taken in rapid succession just before end), O_2 content of inspired air being respectively about 17.4, 13.8, 10.2 and 6.6 volumes per cent. Segments G and H were taken three and seven minutes respectively after resuming breathing of room air.

fell. The maximum effect was observed when the oxygen content was at its lowest level. However, the effect of anoxemia was not equally marked in all the subjects.

The contour of the electrocardiogram tended to return toward normal without much lag as soon as the subject resumed breathing room air.

DISCUSSION

The electrocardiographic changes produced in this series of normal subjects by generalized anoxemia resemble those occurring during spontaneous or induced attacks of angina pectoris. It is important to stress

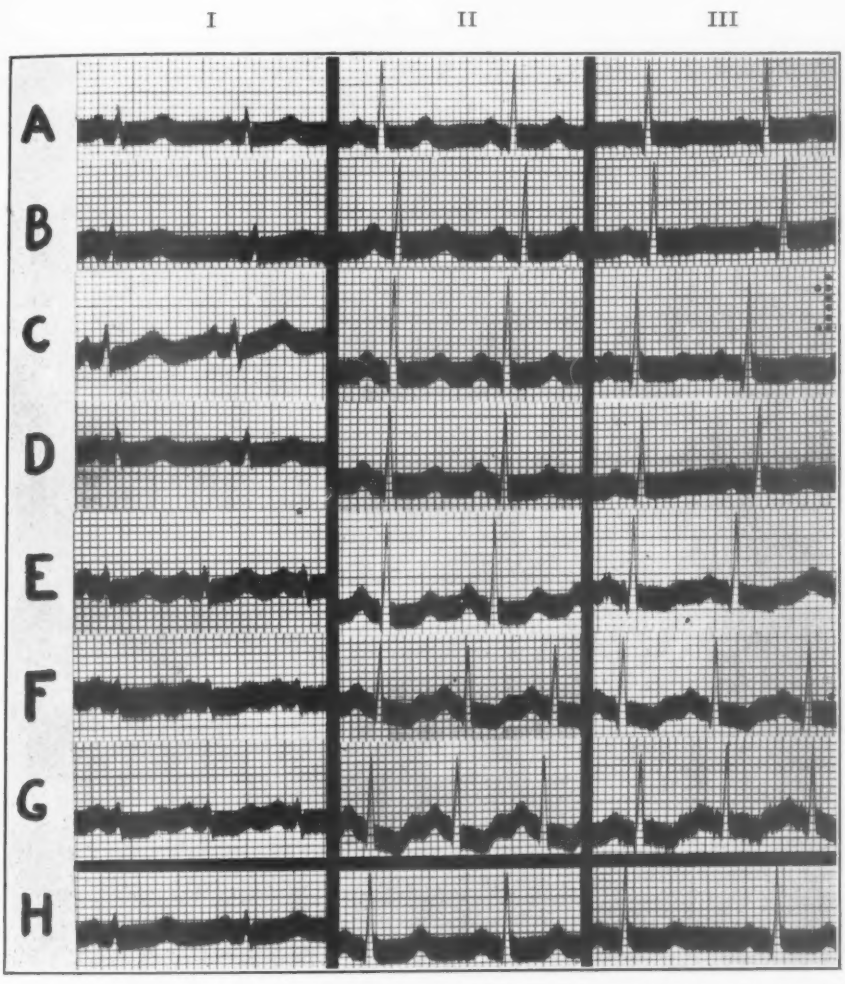

Fig. 4.—Normal subject J.R. Standard three leads of electrocardiogram during induced generalized anoxemia. Segment A, control while breathing room air. Segments B, C, D, E, F and G, successive stages during rebreathing (F and G being taken in rapid succession just before end), O_2 content of inspired air being respectively about 18.5, 16.0, 13.5, 11.0 and 8.5 volumes per cent. Segment H was taken four minutes after resuming breathing of room air.

that these electrocardiographic changes occurred without any symptoms of precordial distress. The rebreathing in every instance was stopped at command of the subject, because of discomfort or when the patient became unconscious. (This latter event occurred in only a few subjects.)

In 6 patients suffering from angina pectoris, who were tested in the same way as the normal subjects, 4 developed electrocardiographic changes similar to those observed in the normal subjects without the appearance of precordial distress. The frequency of precordial pain in this small series of angina pectoris cases is less than that reported by Rothschild and Kissin.[9]

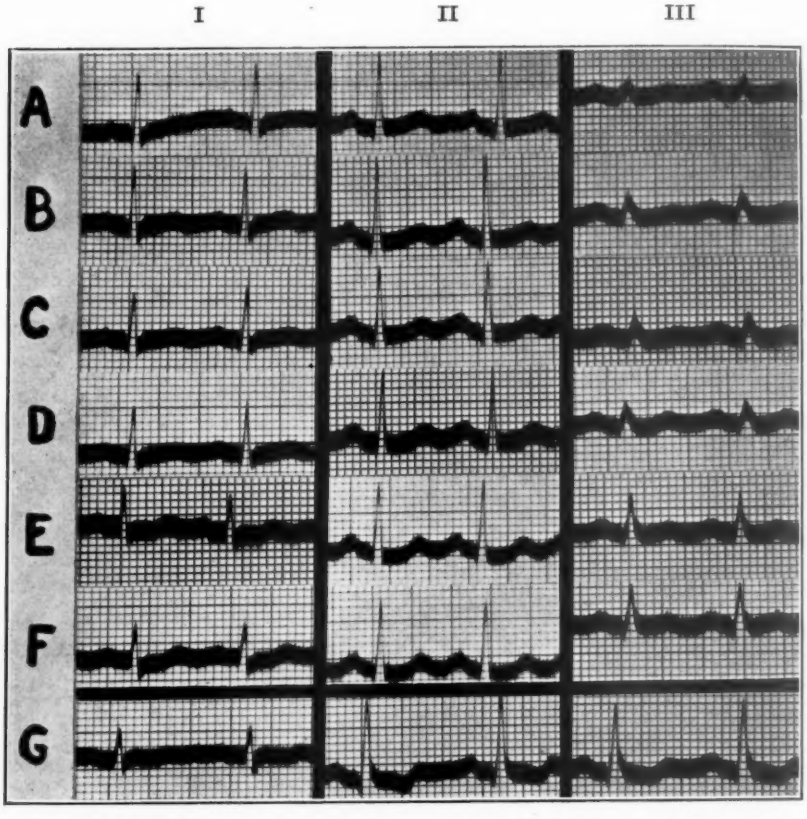

Fig. 5.—Subject T.P. (angina pectoris). Standard three leads of electrocardiogram during induced generalized anoxemia after which patient developed anginal pain. Segment A, control while breathing room air. Segments B, C, D, E and F, successive stages during rebreathing (E and F being taken in rapid succession just before end), the O_2 content of inspired air being respectively approximately 18.0, 15.0, 12.0 and 9.0 volumes per cent. However, no analysis of inspired air was made at end of rebreathing. Segment G was taken five minutes after resuming breathing of room air. Note the right axis shift in this patient which persisted and increased even after breathing of room air was resumed; the record taken after resuming breathing of room air shows other abnormalities.

Our results emphasize the fact that while anoxemia (and cardiac ischemia) consistently tends to produce characteristic electrocardiographic changes, it does not lead inevitably to attacks of anginal pain. It has been definitely established by work in this laboratory by Kissin[15] and Perlow, Markle and Katz[16] that generalized anoxemia will cause pain in an exercising normal skeletal muscle. There is also no doubt

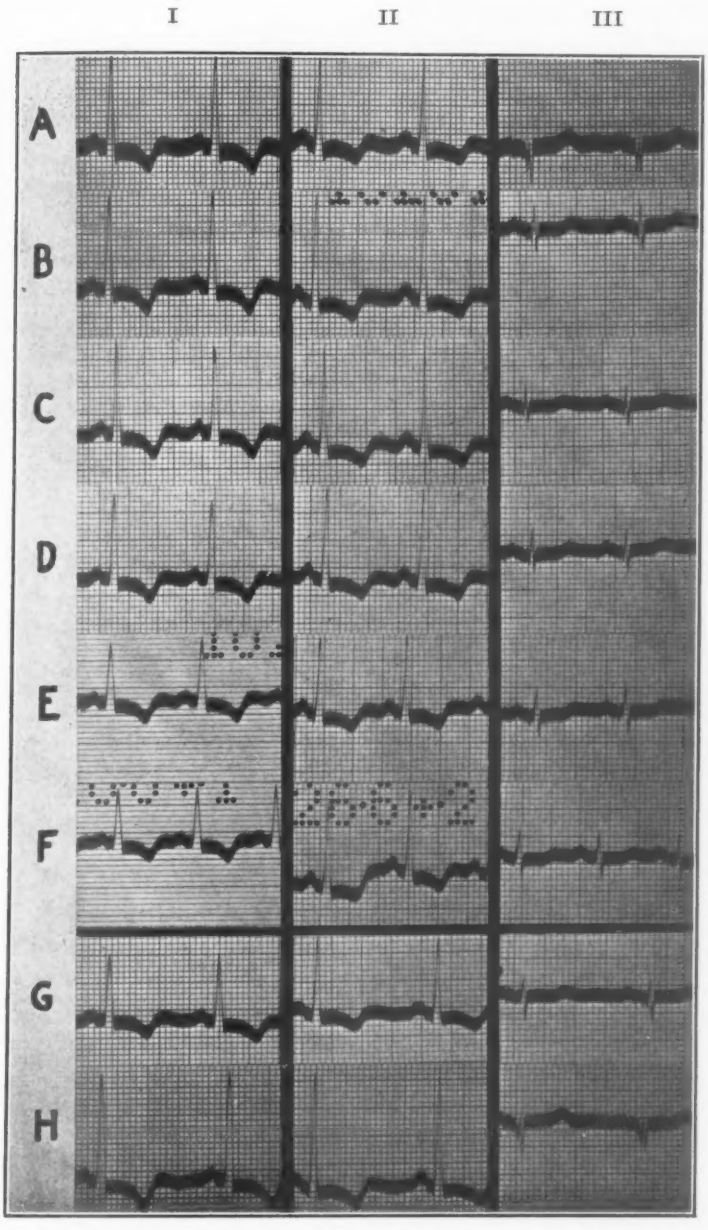

Fig. 6.—Subject W.A. (angina pectoris). Standard three leads of electrocardiogram during induced generalized anoxemia during which patient developed anginal pain. Segment A, control while breathing room air. Segments B, C, D, E and F, successive stages during rebreathing, O_2 content of inspired air being respectively approximately 18.4, 15.7, 13.0, 10.3 and 7.6 volumes per cent. Segments G and H were taken four and thirty minutes respectively after resuming breathing of room air.

that generalized anoxemia may precipitate an attack of angina pectoris in patients suffering from this disease, as was shown by Rothschild and Kissin[9] and Dietrich and Schwiegk[17] and in two of the patients tested

by us. Nevertheless, generalized anoxemia as severe as the above fails to produce attacks of anginal pain in normal subjects and in some patients suffering from angina pectoris, even though the electrocardiographic changes produced resemble those seen where attacks of angina pectoris are brought on by anoxemia. Some other process besides anoxemia (or ischemia) therefore seems to be required for the appearance of attacks of anginal pain. This factor is absent during the time of rebreathing in the normal subjects and in some of the patients with angina pectoris.

It seems to us that this variable is the condition of the nervous system, either of the end organs in the heart, of the afferent pathways to the brain, or of the sensorium of the subject. Our knowledge at present is too meager to define with any degree of accuracy what factors are concerned in affecting these parts of the nervous system. This variable factor prevents the accurate prediction of the occurrence of pain during generalized anoxemia in patients suffering from angina pectoris.

Since pain is not always induced by generalized anoxemia in patients with angina pectoris, apparently this is not an accurate test for this disease. The induction of severe generalized anoxemia throws an undue strain on the heart, especially in patients with cardiac disease, and may be a serious hazard to the patient. The procedure gives diagnostic information in only a small proportion of the cases of angina pectoris and should be undertaken in patients with heart disease only with full realization of the risk involved.

SUMMARY

It was found that the induction of generalized anoxemia in normal subjects produced a diminution in the amplitude of the T-wave, at times leading to its inversion. At the same time the S-T segment was depressed and at times became negative. Similar changes were produced by generalized anoxemia in patients suffering from angina pectoris. These electrocardiographic changes occurred without the appearance of anginal pain in the normal subjects and in four of six patients suffering from angina pectoris. However, two of the six patients with angina pectoris did develop typical mild anginal pain.

It is therefore concluded that some process in addition to anoxemia (or ischemia) is concerned in the production of the pain of angina pectoris. This process is a variable which prevents the accurate prediction of the occurrence of pain during induced anoxemia. Because of the variability in the results and of the hazard to the patient, the use of induced anoxemia as a test for the presence of angina pectoris is of questionable value.

We are indebted to the volunteers who acted as subjects for this study.

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ELECTROCARDIOGRAPHIC OBSERVATIONS ON THE CAROTID SINUS REFLEX

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THE electrocardiographic manifestations of direct vagal stimulation have been studied experimentally in animals by Rothberger and Winterberg,[1] Einthoven and Wieringer,[2] Cohn,[3] Lewis,[4] and others. Although their observations varied somewhat in detail, in the main their conclusions were the same. The usual findings were sinus slowing, sino-auricular standstill and varying degrees of heart-block, from mere delay to complete dissociation. Occasionally, shifting of the pacemaker from the upper to the lower end of the sinus node was observed. Ectopic foci of impulse formation developed in some cases, resulting in auricular or ventricular escape from vagal inhibition. The ventricular portion of the conduction apparatus was rarely influenced by vagal stimulation. Increased height of the R-wave and diminished height of the T-wave were occasionally induced. In general the right vagus nerve had its main effect on the inhibition of the impulse formation, while that of the left was on the auriculoventricular conduction.

Comparatively few electrocardiographic studies of the vagal effect upon the human heart are recorded in the literature. The findings of those reported are in general the same as those seen in experimental animals. Robinson and Draper[5] induced vagal effect by "pressure on the vagus nerve in the neck." They found inhibition to the impulse formation and occasional increase in the R-wave to be the usual right pressure effects. Left effects were mainly those of delay in auriculo-ventricular conduction, and occasional decrease in the R-wave. The T-wave was slightly flattened. No significant changes were found in the P-wave. Levine[6] induced his vagal effect by the oculocardiac reflex. Pressure on the right eye induced occasional changes in the P-wave with frequent inhibition of the sino-auricular node. Pressure on the left had more effect on the auriculoventricular conduction. Wilson[7] reported a case showing abnormal ventricular complexes and nodal rhythm on vagal stimulation. I[8] reported a case of partial bundle-branch block in which reflex vagal stimulation produced normal ventricular complexes. This was attributed, however, to slowing of the heart with its resultant recuperative effect on the interventricular conduction apparatus and not to direct effect of the vagus on that apparatus. Laslett[9] found no marked difference in the effects of the two nerves. Slowing occurred in the proportion of 68 to 55 for right and left nerves respectively. Prolonged conduction occurred in the proportion of 15 to 23 for the right

and left nerves. Kleeman's[10] findings were about the same. Ritchie[11] found the inhibitory effect of the left vagus to be less than that of the right, both on rate and on conduction, in a case of auricular flutter with transient fibrillation.

In previous communications[12, 13, 14] I reported the results of a clinical study of the carotid sinus reflex in a series of 345 cases. Electrocardiograms were made on a number of these cases immediately before and during the time the reflex was induced. This paper deals with an analysis of fifty representative electrocardiograms in this series. The reason why the findings in only 50 cases are reported, is that only these cases had been observed for a considerable length of time. Each had had at least two electrocardiographic examinations on previous occasions and one just before the carotid sinus reflex was elicited. This precaution was taken to rule out the possibility of any electrophysiological disturbances that might have occurred without the reflex. In each case, the electrocardiographic effects of the reflex were immediate and definite and lasted only during the period such reflex was induced. A response could be produced in each case only by the reflex.

ANALYSIS OF FINDINGS

Each electrocardiogram was obtained first in the three standard leads before carotid sinus pressure. The lead showing the highest deflection was then chosen for study of the effects of such pressure. About 8 to 12 deflections were recorded for each of the right and left vagal effects. In the majority of cases only the first 8 deflections showed any deviations from the original tracing. In each tracing obtained before and after carotid sinus pressure, the interauricular and interventricular time intervals and auriculoventricular conduction time were calculated. Likewise, the new rhythm and any new features that developed were noted. Thus any auricular and ventricular slowing, acceleration, auriculoventricular conduction disturbances and other abnormalities could be seen at a glance from the figures obtained. The findings obtained by carotid sinus pressure were further classified according to the form of disturbance of impulse formation and conduction and the changes that occurred in the auricular and ventricular complexes. Table I is a summary of this classification.

The predominant vagal effect obtained was slowing of the entire heart. In this respect left carotid sinus pressure showed more frequent response than did the right. Complete stoppage of the heart occurred twice as frequently with right as with left carotid sinus pressure. Mild grade auriculoventricular block occurred as frequently with right as with left carotid sinus pressure. High degree block (Fig. 1) occurred more than twice as frequently with left carotid pressure as with right. A curious finding was a shortening of the auriculoventricular conduction

time, which was obtained twice with right and once with left pressure effect. Variations in the normal auriculoventricular conduction time even in the same case were frequent. This occurred about three times as often with right as with left carotid sinus pressure. Ventricular escape from inhibition (Fig. 5) as well as nodal rhythm (Fig. 3) were occasionally observed. Sinus arrhythmia associated with sinus slowing was an occasional finding (Fig. 2).

TABLE I

SUMMARY OF ELECTROCARDIOGRAPHIC FINDINGS OBTAINED IN RIGHT AND LEFT CAROTID SINUS PRESSURE

	RIGHT	LEFT
Sinus Slowing—Simple	14	14
With S. A.	5	7
With A-V. B.	2	3
With A-V. B. and V. E.		2
With S. A. and A-V. B.	1	2
Total Showing Sinus Slowing	22	28
S-A. Standstill and Sinus Slowing	10	3
With S. A.	5	
With N. R.	2	2
With V. E.	2	1
With A-V. B.	1	4
Total Showing S-A. Standstill	20	10
A-V Conduction		
Variations, but within normal limits	20	6
Diminished	2	1
Prolonged and variable	4	4
High degree block	5	12
CHANGES IN COMPLEXES		
P-Wave		
Diminished	10	5
Nearly isoelectric	5	7
Negative	1	1
Notched	1	
R-Wave		
Increased	6	3
With decreased S-wave	1	
Decreased	4	3
Prolonged QRS		2
R-T and S-T Segment rounding or depression	3	1
T-Wave		
Increased	1	
Decreased	1	3
Premature Contraction	2	3
Shifting Pacemaker	1	

The figures show the number of cases with respective responses. Some cases showed response to both right and left pressure. Others showed one type of response on right, and another type on left pressure. Still others showed only one-sided response.

S. A. = sinus arrhythmia.

V. E. = ventricular escape.

A-V. B. = auriculoventricular block.

N. R. = nodal rhythm.

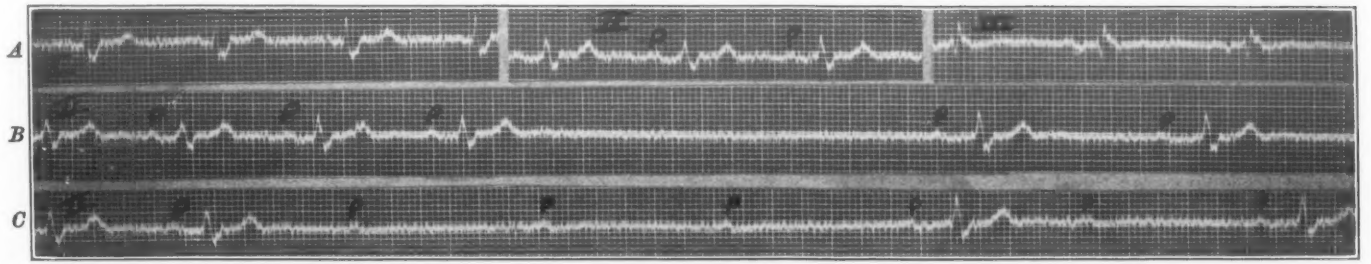

Fig. 1.-*A*, Tracing in the first, second, and third leads obtained before carotid sinus pressure was applied. Low voltage, slurred and notched QRS. Delay in auriculoventricular and interventricular conduction time.

B, Second lead on right carotid sinus pressure. Sino-auricular standstill, sinus slowing and slight increase in delay of auriculoventricular conduction time.

C, Same lead on left carotid sinus pressure. Slight sinus slowing with complete auriculoventricular block followed by increase in delayed conduction.

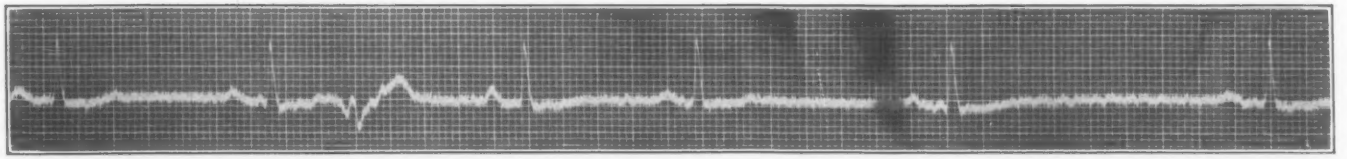

Fig. 2.—Obtained on left carotid sinus pressure. Sinus slowing and sinus arrhythmia. Delay in auriculoventricular conduction time in various degrees. Variations in shape and size of P-waves.

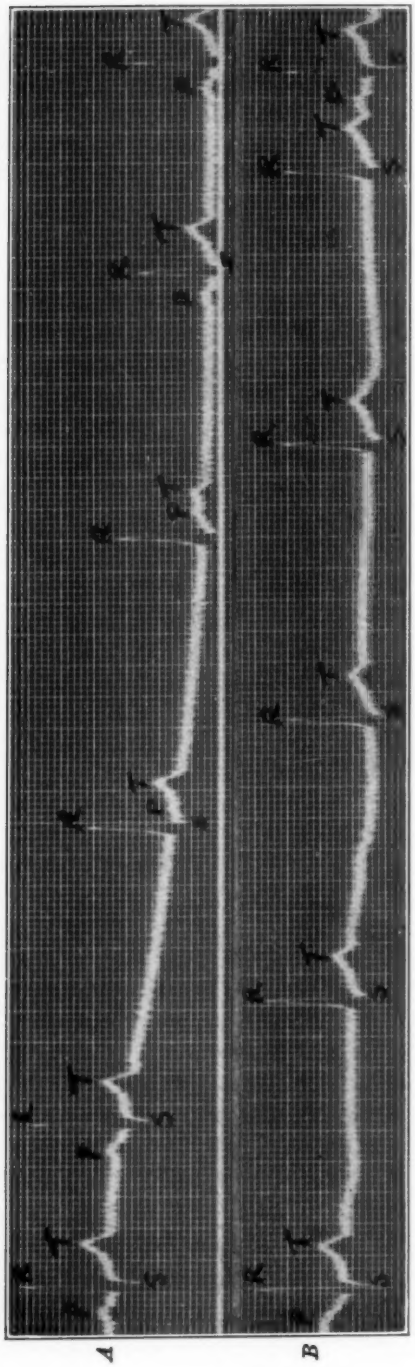

Fig. 3.—Tracing obtained on right (*A*) and left (*B*) carotid sinus pressure. *A* shows two normal complexes followed by two complexes of nodal origin. There is then a resumption of the regular sinus rhythm at a slower rate than previously. The R-waves are shorter. *B* shows sino-auricular standstill which lasted about 7.68 seconds with four ventricular complexes of nodal origin. The first of the auricular and ventricular complexes following the nodal rhythm occurs prematurely with delay in auriculoventricular conduction time.

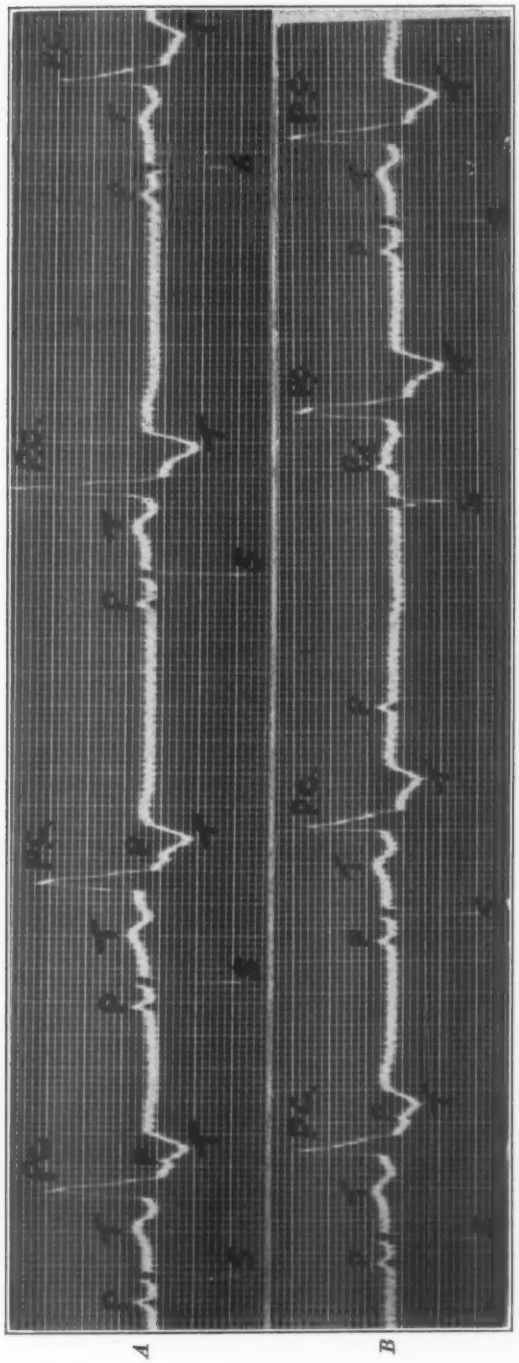

Fig. 4.—Complexes obtained on right (*A*) and left (*B*) carotid sinus pressure. *A*, Every normal ventricular complex is followed by a ventricular premature contraction. There is a gradually increasing sinus slowing with the auricular waves falling on the ventricular premature contractions in the first two complexes. *B*, Sinus slowing is less marked and auriculoventricular block occurs after the second premature contraction; there is then a ventricular complex of superventricular origin with auricular impulse of sinus origin following it.

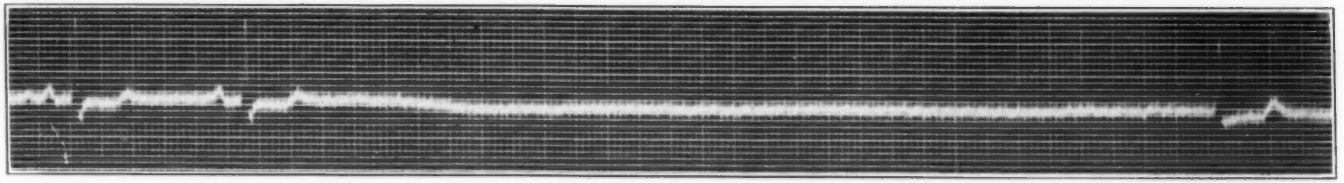

Fig. 5.—Tracing obtained on right carotid sinus pressure. Sino-auricular standstill for 7.6 seconds with ventricular escape. Diminished R-wave and increased T-wave following standstill.

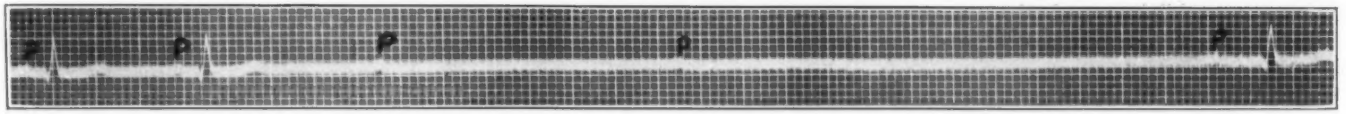

Fig. 6.—Tracing obtained on left carotid sinus pressure. Sinus slowing, sino-auricular standstill, and auriculoventricular block.

Changes in the auricular complexes were rather frequent. These varied from mere lowering in voltage of the P-wave to its almost entire disappearance. Occasionally the P-wave became negative (Fig. 7) or notched (Fig. 6). These changes occurred somewhat more often on right than on left carotid sinus pressure. The variations in the P-wave usually occurred for only from one to five deflections and were more frequent after sinus standstill.

Changes in the initial ventricular complexes occurred less frequently. The R-wave was almost as often decreased as increased, and either change was slightly more frequent on right than on left sinus pressure. R-wave changes occurred usually after a prolonged standstill. Changes in the R-T and S-T segments as well as in the T-wave occurred very rarely and were slight in degree. They usually followed changes in the R-wave.

Ventricular premature contractions were noticed twice on right and

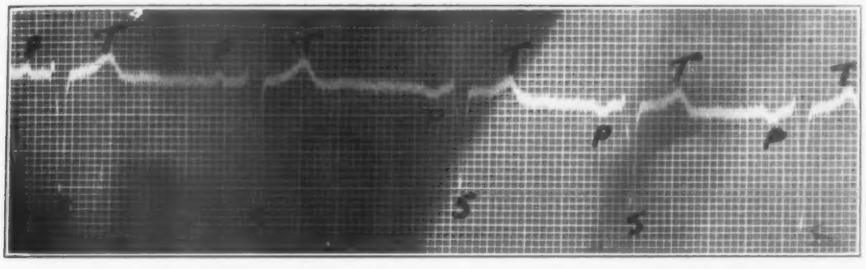

Fig. 7.—Tracing obtained on left carotid sinus pressure. The first two impulses are of normal sinus origin. The last three are of an ectopic origin.

twice on left carotid sinus pressure. In one case there occurred a sinus premature contraction on left carotid sinus pressure (Fig. 3 *B*).

Pulsus bigeminus was produced in one case (Fig. 4 *A* and *B*) when the rate slowed. This case, however, had shown this abnormality once before, without carotid sinus pressure. The accompanying disturbances in impulse formation and conduction had never occurred before. In two cases of auricular fibrillation carotid sinus pressure produced auriculoventricular block with ventricular slowing or standstill. The fibrillation was not influenced by such pressure.

COMMENT

The observations presented in this paper confirm previous reports of the similarity in the vagal effects on the human and on animal hearts. The main effects are those of interference with the impulse formation in the sino-auricular node and its propagation along the auricles and conducting apparatus. Although the vagal effects are reflex in origin, and we cannot therefore accurately gauge in this way the relative right and left effects, the similarity of response in humans to that obtained by

direct vagal stimulation in animals leads us to believe that the predominant reflex effect is homolateral. If this be correct, our findings indicate that both the formation and propagation of the impulse are controlled by both vagi alike, the difference being only in degree. Apparently right vagal terminals are found in greater number in the sinus node, and left terminals in the auriculoventricular nodal area. Both vagal endings are, however, found in both locations. The variations in form of response in different individuals apparently depend upon differences in the distribution of the vagal endings in the respective hearts. Anatomical, physiological, and chemical disturbances at the terminals of the vagal endings may also play a part in influencing the response. The disturbances in the appearance of the auricular complexes observed in many cases on vagal stimulation are undoubtedly due to focal interference with the normal impulse propagation along the auricles, and imply the presence of vagal terminals in the auricular walls in varying numbers.

The ventricular complexes are affected apparently little by the vagal impulses. Our findings do not corroborate those of Robinson and Draper,[5] who report an increased R-wave on right and a decreased one on left vagal stimulation. No prediction can be made as to the character of the R-wave obtainable by vagal stimulation. Changes in the R-T and S-T segments were not described by any of the authors mentioned in this paper. We found such changes only in four instances. The T-wave is likewise very seldom affected. Although Garey[15] produced the appearance and disappearance of the T-wave by local application of atropin to the various parts of the ventricles, reflex vagal stimulation affects the T-wave very little. This may be due to comparatively few vagal nerve endings in the ventricular walls of most individuals and the inability to influence conduction in the greater muscle mass of the ventricles in most cases.

SUMMARY

Fifty electrocardiograms obtained on carotid sinus pressure showed the predominant vagal effects on the heart to be sino-auricular slowing or standstill and various grades of auriculoventricular block. Right carotid sinus pressure had a greater tendency to produce complete standstill. Left pressure had a greater tendency to produce complete auriculoventricular block. Ventricular escape from vagal inhibition, nodal rhythm and sinus arrhythmia occasionally occurred. P-wave changes were frequent and R-wave changes were less frequent. R-T segment and T-wave changes occurred comparatively rarely. It is suggested that the variations in response of the right and left nerves, as well as the difference in response in the different hearts, are dependent upon variations in the number of vagal terminals of the respective nerves in various portions of the heart.

I am indebted to Louis Gurian for his valuable assistance in the work connected with this paper.

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THE ACTION OF QUININE AND QUINIDINE ON PATIENTS WITH TRANSIENT VENTRICULAR FIBRILLATION*†

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THE purpose of this study was to determine the clinical manifestations and the successive changes in the rhythm of the heart following the intravenous administration of graded doses of quinine dihydrochloride and quinidine sulphate to patients with auriculoventricular dissociation subject to transient seizures of ventricular fibrillation. These drugs have been used both orally and intravenously with moderate success in the treatment and prevention of certain forms of the transient types of ventricular tachycardias.[1-5] Their administration in one form or another has been strongly advocated in the treatment and prevention of transient seizures of ventricular fibrillation on the ground that the frequency of such seizures would be greatly diminished by their use.[6] Indeed, it has been suggested by Morawitz[7] and others[8, 9] that quinidine might be used with success as a prophylactic drug in patients regarded as liable to sudden death as a result of ventricular fibrillation.

The assumption that these drugs would be of therapeutic value in such patients seems to us to be based on very meager clinical experience, and in fact mostly on hypothesis. For while both quinine[10, 11] and quinidine[12] have been demonstrated to have an inhibitory effect upon ventricular fibrillation produced in the experimental animal as a result of timed electrical stimuli, such transfers of practice are not applicable to human beings. On the contrary, it would appear from the very few clinical reports in the literature that quinidine may result in the development of transient ventricular fibrillation.

REVIEW OF LITERATURE

In 1921, Kerr and Bender[13] reported observations on a male, sixty-eight years of age, who was observed over a year, during which time there were several attacks of cardiac syncope following the administration of quinidine sulphate. Electrocardiograms obtained during some of these attacks revealed transient ventricular fibrillation. They concluded that quinidine therapy was dangerous in such patients.

Unfortunately, some of their observations were made at a time when the ventricular rate varied between 40 and 70 beats per minute and when the ventricular rhythm was totally irregular. It is well established

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from our previous studies[14] that when the basic ventricular rate in such patients behaves in this manner, syncopal attacks due to transient ventricular fibrillation may occur easily and spontaneously without the use of any drug.

Dock[6] reported a male, aged thirty-six years, suffering from syncopal attacks that increased in frequency within one year. An electrocardiogram obtained at the end of one of these attacks revealed a ventricular arrhythmia with a rate of 285 beats per minute which, in his opinion, was ventricular fibrillation. He found that quinidine sulphate rationing prevented these attacks, although the patient still suffered from an occasional seizure during the following year. Although Dock's patient was apparently free from syncopal attacks due to transient ventricular fibrillation, it is very likely that if more electrocardiograms had been obtained in the year following his hospital admission, the basic rhythm would have revealed a pre-fibrillatory mechanism at some time or other during that period. In studying such patients one cannot rely solely upon the absence of syncopal attacks as a measure of the efficacy of a drug. Quinidine administered orally may produce a constant ventricular irregularity without ending in syncope, especially in the doses used by Dock. Without controls of the rhythm over long periods of time, it is difficult to evaluate the beneficial effects of the drug.

Davis and Sprague[15] reported recurrent seizures of ventricular fibrillation in the course of quinidine therapy (123 grains in four days) in a woman whose basic rhythm prior to the use of the drug showed auricular fibrillation with bigeminal rhythm due to alternate premature ventricular beats. Again, in view of the fact that such a bigeminal rhythm may be the characteristic feature of the pre-fibrillatory mechanism in the spontaneous development of such seizures, it is unfair to incriminate the drug as responsible for these attacks. The ventricular fibrillation in their patient may have been a terminal phenomenon such as we have recently described in another patient.[16]

Finally, Escamilla[17] observed a sixty-year-old male suffering from transient seizures of ventricular fibrillation to whom he administered quinidine at various intervals. Although he concluded that quinidine was of some value in his patient, he observed that the effect was not invariable enough to enable him to draw any absolute conclusions as to its efficacy. It is obvious from a review of the protocol of his case that adequate control studies of the ventricular rate and rhythm prior to or during the administration of quinidine are totally lacking. With these points in view, we attempted the following experiments.

METHOD OF STUDY

Two patients with auriculoventricular dissociation who were suffering from recurrent transient seizures of ventricular fibrillation form the subjects of this study. The natural course of the development of their

attacks and the successive changes in the rhythm of their hearts were studied by us carefully over a period of several years. During this entire time they were in the Montefiore Hospital, and hundreds of correlated observations were made on their heart rhythms at the same time that electrocardiograms were obtained.

These experiments were carried out at a time when it was certain that the patients had not had any transient seizures of ventricular fibrillation for at least twenty-four hours. It was definitely determined from constant study of both the heart rate and the pulse, with the patients attached in the electrocardiographic circuit, that the basic ventricular rate was fairly constant for at least four hours prior to the onset of an experiment. A basic ventricular rate that was almost regular and did not vary more than five beats per minute was considered an essential condition before initiating an experiment. When the basic rhythm was interrupted spontaneously by the appearance of premature ventricular beats, the number of such extrasystolic contractions was counted each minute for at least ten minutes prior to the use of any drug. The patients were kept in bed all the time, and no other medication was administered to them throughout the entire period of these studies. In one instance inhalations of amyl nitrite were given after quinidine had been used.

On several occasions and frequently before the drugs were used, the effects of the intravenous injection of 1 c.c. of either distilled water or physiological saline were determined in order to rule out any abnormal changes in the rhythm of the heart or in the complexes of the electrocardiograms that might follow the injection of the fluid itself.

One of us timed the clinical manifestations following the injection of the drugs, while the other recorded the time intervals at which changes appeared in the electrocardiograms. All studies were carried out with Lead II only. Successive changes in the rhythm of the heart were recorded as frequently as it was thought necessary, and observations of the movements of the galvanometer string were followed for several hours after the use of the drug unless the condition of the patient made it impossible to do so, in which case reliance was placed solely upon the clinical manifestations.

The minimal dose of the drugs that was necessary to produce transient changes in the rhythm of the heart was arrived at by the method of trial and error. Starting with very minute quantities, the dosage was gradually increased in repeated preliminary experiments until it was determined how much was needed to produce a pharmacological effect. The final amount used was based on the average amount required to give a specific effect.

Although innumerable observations were made from time to time, we have thought it advisable to describe only some of the typical protocols.

Each one of these demonstrates some mode of action of the drugs to which we direct particular attention. Since the effects on the heart rhythms have been somewhat variable each time, the sequence of the experiments has been rearranged so as to form a consecutive story. Before describing these alterations, however, it is important to call attention to the successive changes in the cardiac mechanism which take place when transient ventricular fibrillation develops spontaneously in patients with auriculoventricular dissociation so that comparisons can be made with such alterations in the rhythm of the heart which may be attributed to the influence of the drugs.

THE ALTERATIONS IN THE RHYTHM OF THE HEART PRECEDING TRANSIENT PERIODS OF VENTRICULAR FIBRILLATION

The alterations in the rhythm of the heart that precede transient periods of ventricular fibrillation during the presence of auriculoventricular dissociation are effected through (a) an increase in the basic idioventricular rate and (b) the interposition of premature ventricular beats either singly or in groups. These eventually lead to the development of short recurrent runs of aberrant ventricular oscillations which, in the final analysis, are short runs of ventricular fibrillation.

The basic idioventricular rate may at times be accelerated in the prefibrillatory period, and this acceleration may be brought about through a variety of mechanisms which have already been described elsewhere.[18, 19] Obviously, the effects of any drug upon the cardiac mechanism in patients with auriculoventricular dissociation must first take into account the inherent variability of the idioventricular pacemaker in such patients at a time when they are free from symptoms due to transient ventricular fibrillation.

Prolonged observations on our two patients during their "quiescent" periods, when they are free from symptoms, revealed that there was a marked fixation of the inherent ventricular rate from day to day and at times from month to month. In both cases the average ventricular rate of from 27 to 31 beats per minute did not vary more than 5 beats per minute at the most at any one time. This relatively "fixed" ventricular rate was found to be the same during deep sleep as well as during undue exertion, excitement, or emotional disturbance. Respirations did not affect it and the use of adequate doses of atropine sulphate (gr. 1/120 intramuscularly) did not influence it, indicating that at such times the auriculoventricular pacemaker in them was not regulated by the extrinsic cardiac nervous mechanism. In both of these patients, when the increase in the basic ventricular rate appeared prior to the development of a transient seizure of ventricular fibrillation, the changes in the rate were gradual. Occasionally, such variations were easily appreciated by the patients, who complained of precordial distress. In

these periods of well-being, therefore, the idioventricular rates may be said, for practical purposes, to have been constant.

The changes in the rate of the idioventricular pacemaker in themselves are not sufficient to precipitate the type of ventricular fibrillation with which we are concerned. Sooner or later, either in the presence of a basically accelerated ventricular rate or frequently in its absence, premature ventricular beats begin to appear. These may at first alternate so as to produce a typical bigeminal rhythm, or they may increase in frequency before the interposition of aberrant ventricular oscillations begins to disrupt the rhythm. These ventricular oscillations can be appreciated clinically by the fact that only the first few beats associated with them are audible at the apical portion of the heart or palpable at the wrist. They are so frustrate in character that they are insufficient to open the aortic orifice, and consequently cerebral anemia sets in when they last for a period longer than from eight to ten seconds. If they last as long as forty seconds or more, a typical Stokes-Adams seizure occurs, with pallor of the skin and face, unconsciousness, stertorous breathing, incontinence of feces and of urine, a drop in blood pressure, and finally apnea, with intense cyanosis due to asphyxia. None of these phenomena has ever been seen to appear without the previous interruption of the basic idioventricular rhythm by recurrent short periods of ventricular oscillations which, in their final analysis, are short runs of ventricular fibrillation. Similar alterations in the cardiac mechanism have never been observed by us to follow the intravenous injection of either distilled water or physiological saline solution.

THE EFFECTS OF GRADED DOSES OF QUININE DIHYDROCHLORIDE IN PATIENTS WITH TRANSIENT VENTRICULAR FIBRILLATION

Patients with transient seizures of ventricular fibrillation occurring during auriculoventricular dissociation vary in their response to the same dose of quinine dihydrochloride from time to time. The speed of injection does not influence this in any way when the same dose is used. The immediate result following the injection of quantities of up to ½ c.c. of the solution (1¾ grains of the drug) is usually a sensation of warmth which the patient feels all over the body. At times large beads of perspiration appear on the forehead, and the skin feels moist and clammy. Occasionally a sense of constriction is felt in the midsternal region, and with this there is a short period of restlessness that may be followed immediately by profound disturbances in the rhythm of the heart.

On one occasion, at a time when the basic ventricular rate averaged 31 beats per minute, the administration of ½ c.c. (1¾ gr.) of quinine dihydrochloride resulted in the appearance of only two premature ventricular beats nine minutes after the injection of the drug. However, when an additional dose of only ¼ c.c. (⅞ gr.) was injected forty-five

minutes after the first dose, there was an immediate but transitory increase in both the auricular and the ventricular rates from 100 and 31 beats per minute to 125 and 43 beats respectively. At the same time the ventricular complexes, which had previously been all of the upright form, now became variable in direction, assuming transitional changes from dextrograms to levograms.

One minute later there was a bigeminal rhythm due to premature beats of the ventricles. The auricular rate, however, was now lowered to 100 beats, and four minutes later there was a further reduction in the auricular rate to 83 beats per minute and in the ventricular rate to 26. Within five minutes, however, the rhythm assumed a bigeminy again, and exactly forty-five minutes after the injection of the second dose of the drug a transient period of ventricular fibrillation was ushered in by a pre-fibrillatory mechanism consisting at first of a bigeminal rhythm and then of a few short runs of aberrant ventricular oscillations before a typical Stokes-Adams seizure developed. There were repeated seizures of syncope after this that lasted for not more than one minute each before the rhythm returned to its original basic level of 31 beats per minute, about two and one-half hours after the beginning of the experiment.

On another occasion, after a control period during which the ventricular rate was fairly fixed and averaged 30 beats per minute, the injection of ½ c.c. (1¾ gr.) of quinine dihydrochloride resulted within six minutes in the development of a short pre-fibrillatory mechanism and one minute later in a typical Stokes-Adams seizure due to transient ventricular fibrillation. After recovery from this attack, the patient complained of palpitation of the heart due to irregular beating which, however, lasted only a few minutes before there was a return to the basic idioventricular rhythm with a regular rate of 32 beats per minute. This persisted for approximately one-half hour before another Stokes-Adams seizure appeared. This was ushered in by a few alternating premature beats of the ventricle with a very short run of grouped beats before the major attack developed. For the next hour these abnormal rhythms alternated with the basically regular rhythm until there was finally a restoration to the basic rhythm two hours after the injection of the drug.

A third observation in the presence of a fixed ventricular rate averaging 31 beats per minute was followed within three minutes after the injection of ½ c.c. (1¾ gr.) of the drug by a short run of ventricular fibrillation. There were two similar attacks five and seventeen minutes later, before these abnormal rhythms and their precursory mechanism disappeared altogether. Not until fifty minutes after the injection of the drug was the patient free from any irregularities of the heart. Then the basic rhythm with a ventricular rate of 31 beats per minute returned and remained regular after that.

In another observation, at a time when alternate premature beats of the ventricle constantly interrupted the basic auriculoventricular dissociated rhythm, the injection of variable doses of the drug ranging from ¼ to ½ c.c. resulted within a few minutes in the development of short runs of multiple premature ventricular beats or in the appearance of the pre-fibrillatory mechanism which disappeared, however, within from one-half to one hour after the injection.

In the light of these experiences no attempt was made to try the drug during an actual period of ventricular fibrillation.

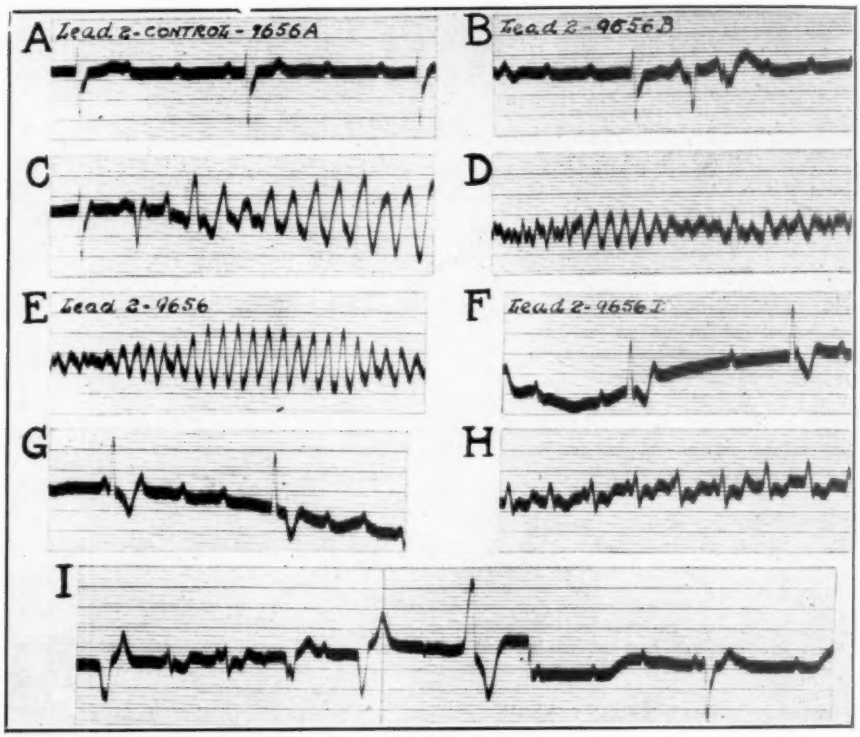

Fig. 1.

Fig. 1.—Portions of continuous strips (Lead II) showing the development of a transient seizure of ventricular fibrillation following immediately the intravenous injection of ⅓ of a grain of quinidine sulphate.

A, Control, the basic ventricular rhythm; *B*, the pre-fibrillatory mechanism; *C*, the mechanism initiating ventricular fibrillation; *D* and *E*, records obtained during a Stokes-Adams seizure; *F* and *G*, the intermediary idioventricular rhythm following ventricular fibrillation; *H*, the post-fibrillatory tachysystole; *I*, the gradual restoration to the basic rhythm.

THE EFFECTS OF GRADED DOSES OF QUINIDINE SULPHATE ON PATIENTS WITH TRANSIENT VENTRICULAR FIBRILLATION

The intravenous injections of 1 c.c. (⅙ gr.) of quinidine sulphate to a patient whose ventricular rate averaged 28 beats per minute and who showed only one premature beat of the ventricles during a control period in which the rate was counted every minute for one and one-

half hours, resulted in the immediate appearance of multiple premature ventricular beats. These premature beats persisted either singly or in groups for the next forty-five minutes, when they gradually disappeared and the basic rhythm returned to normal. On the further injection of 1½ c.c. of the drug (¼ gr.) one-half hour after the first dose, there developed immediately multiple premature beats. Within two minutes there was a short pre-fibrillatory mechanism, and for the next twenty-five minutes there was a constant and fixed bigeminal rhythm due to

TABLE I

CHARACTERISTIC PROTOCOL SHOWING THE SUCCESSIVE CLINICAL AND GRAPHIC MANIFESTIONS FOLLOWING THE ADMINISTRATION OF ONE-THIRD OF A GRAIN OF QUINIDINE SULPHATE. SEPTEMBER 15, 1933, PROTOCOL NO. 2B

TIME	VENTRICULAR RATE	DRUG USED	RHYTHM	COMMENT	EKG. NO.
2:35 P.M.	31		Regular.	Comfortable. No complaints.	
2:40 P.M	29				
2:43 P.M.	30				
2:45 P.M.	31				
2:48 P.M.	31				
2:53 P.M.	33				
2:58 P.M.					9656-A
3:00-3:01 P.M.		Quinidine sulphate (2 c.c. -⅓ gr.) intravenously			
3:01 P.M.			Pre-fibrillatory process and ventricular fibrillation.	Typical Stokes-Adams seizure.	9656-B
3:02 P.M.			Ventricular fibrillation.	Typical Stokes-Adams seizure.	9656-C
3:03 P.M.			Post-fibrillatory period	Unconscious.	9656-D, E
3:03-3:04 P.M.				Unconscious.	9656-F
3:05 P.M.				Screams. Complains of palpitation.	9657-A
3:06 P.M.				Dyspneic.	9658
3:07 P.M.			Recurrent periods of pre-fibrillatory process.		9659
3:08 P.M.					9660
3:10 P.M.					9661
3:11 P.M.				Pulse small, hardly perceptible, gradually increasing in intensity with the return of the regularity of the rhythm.	
3:12 P.M.					9662
3:14 P.M.	32		Regular.		
3:19 P.M.	32		Regular.		
3:20 P.M.				Comfortable.	9663
3:25 P.M.	33				
3:30 P.M.	33			Comfortable.	

alternate premature beats of the ventricles. All abnormalities of the cardiac mechanism disappeared one-half hour after the second injection.

On another occasion (Table I, Protocol No. 2B) the use of 2 c.c. of the drug (⅓gr.) resulted in the immediate development of a Stokes-Adams seizure due to a period of ventricular fibrillation (Ekg. No. 9656-B) that lasted for over one and one-half minutes.

These examples will suffice to point out the rapidity with which the effects of quinidine sulphate appear in contradistinction to those following quinine dihydrochloride.

These observations reveal then that both quinine and quinidine administered intravenously in relatively small doses to patients suffering from transient seizures of ventricular fibrillation result in the development of irregularities of the heart that lead to syncopal attacks, all due to ventricular fibrillation. There is no need to assume that the oral administration of these drugs can likewise lead to similar irregularities instead of abolishing them as has been thought by some. It takes much longer for these drugs to be absorbed by the oral route and to show their effects on the cardiac mechanism. Such studies are at present in progress and will be reported later.

The action of both quinine and quinidine on the ventricles being as complex as it is, no attempt is made at present to offer any explanation for the manner in which these drugs initiate the irregularities leading up to transient ventricular fibrillation.

SUMMARY AND CONCLUSIONS

1. Quinine dihydrochloride and quinidine sulphate were administered intravenously in graded doses to two patients with auriculoventricular dissociation who were subject to transient seizures of ventricular fibrillation.

2. The drugs were injected at a time (a) when the basic idioventricular rate did not vary more than five beats per minute over a period of several hours prior to their use, and (b) when premature ventricular beats interrupted the basic rhythm. The number of these was counted for each minute during the hour preceding the injections., The tests were carried out at a time when it was definitely known that the patients had been free from syncopal seizures for at least twenty-four hours prior to the injections of the drug.

3. It was determined that such patients with transient seizures of ventricular fibrillation responded variably to the same dose of both quinine dihydrochloride and quinidine sulphate at different times.

4. The intravenous administration of small doses of quinine dihydrochloride (maximum dose: 1¾ grains) and quinidine sulphate (maximum dose: ⅓ grain) resulted in the development of either a prefibrillatory mechanism or transient periods of ventricular fibrillation within from one to nine minutes after the injection.

5. Once the pre-fibrillatory mechanism is precipitated by the administration of the drug, recurrent periods of transient ventricular fibrillation may follow for several hours at a time.

6. The intravenous injection of these drugs resulted in a more rapid appearance of ventricular fibrillation when premature ventricular beats were already present prior to the onset of the experiment.

7. Since the intravenous use of these drugs precipitated transient periods of ventricular fibrillation in patients who are subject to such seizures, the use of such drugs by this method is contraindicated in such patients.

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VENOUS PRESSURE IN THYROID DYSFUNCTION*

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SIGNIFICANT variations in venous pressure have been described in congestive heart failure, ascites, arterial hypertension, local obstruction to venous return, certain endocrine disturbances, pregnancy, and various experimental conditions. There are comparatively few reports on venous pressure in thyroid dysfunction, and the recorded observations which are available are meager and contradictory. L. Payan, E. Giraud, and M. Assada[2] injected thyroid extract intramuscularly and noted variable changes in venous pressure. A temporary fall was usually observed when signs of thyrotoxicosis were well developed. M. Villaret, F. Saint Girons and L. Justin-Besancon[3] note briefly that they usually found an elevation of venous pressure in a few cases of Basedow's syndrome. V. Jonas[1] studied 43 patients with hyperthyroidism and found an elevation in venous pressure in 26 (60 per cent), in some of whom the pressure returned to normal when the thyroid symptoms were improved. Some of these patients showed variable degrees of cardiac failure. There appeared to be no correlation between the height of arterial and venous pressures in this series.

PRESENT STUDY

Our material consisted of thirteen patients with definite evidence of Basedow's syndrome and two with myxedema. None of the Basedow patients showed evidence of cardiovascular embarrassment, and only one of the myxedema patients (M. W.) complained of dyspnea on exertion. Basal metabolic rates, pulse rates, systolic and diastolic pressures and venous pressures were determined in all patients. Blood pressure was estimated by the auscultatory method with the patient in the supine position; a mercury sphygmomanometer was employed. Venous pressure was determined by the direct method using a hollow needle inserted into the median basilic vein and connected with a suitable water manometer. The entire system was filled with a sterile 3 per cent sodium citrate solution in order to hinder clotting. The solution was permitted to run into the vein in small amounts at frequent intervals in order to test the patency of the needle. The usual precautions of keeping the patients under basal conditions in estimating venous pressures were observed. The final reading was made

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when the fluid in the manometer was stabilized and the height of the column was practically the same after at least three attempts were made at intervals of a few minutes. A summary of the results obtained may be seen in Table I.

TABLE I

PATIENT	BASAL METABOLIC RATE	BLOOD PRESSURE IN MM. OF MERCURY	PULSE	VENOUS PRESSURE IN MM. OF 3 PER CENT SODIUM CITRATE SOLUTION
		Basedow's Syndrome		
F. Y.	plus 52%	148/ 90	96	64
M. O.	plus 40%	124/ 50	112	80
C. W.	plus 63%	180/120	108	90
E. O.	plus 45%	154/ 76	108	82
M. B.	plus 56%	172/ 78	120	77
M. K.	plus 27%	120/ 88	92	90
G. W.	plus 31%	130/ 62	108	72
C. K.	plus 32%	138/ 84	116	70
J. B.	plus 23%	155/ 75	128	55
S. L.	plus 48%	120/ 80	104	102
H. S.	plus 30%	124/ 78	108	69
A. S.	plus 62%	160/ 90	116	50
F. D.	plus 38%	140/ 90	100	67
		Myxedema		
M. W.	minus 34%	140/ 90	64	95
G. H.	minus 48%	110/ 80	44	52

Five of the patients with Basedow's syndrome were subsequently subjected to subtotal thyroidectomy, and similar studies were made after the basal metabolic rates became stabilized at a normal level. Both myxedema patients were given sufficient thyroid extract to elevate the basal metabolic rate, in one of them to a normal level, in order to

TABLE II

PATIENT	BASAL METABOLIC RATE		BLOOD PRESSURE IN MM. OF MERCURY	PULSE	VENOUS PRESSURE IN MM. OF 3 PER CENT SODIUM CITRATE SOLUTION
	Basedow's Syndrome Before and After Thyroidectomy				
F. Y.	Before operation—	plus 52%	148/ 90	96	64
	After operation—	plus 2%	150/120	92	75
M. O.	Before operation—	plus 40%	124/ 50	112	80
	After operation—	plus 10%	114/ 66	112	65
C. W.	Before operation—	plus 63%	180/120	108	90
	After operation—	plus 7%	168/110	78	75
E. O.	Before operation—	plus 45%	154/ 76	108	82
	After operation—	minus 10%	152/104	72	85
M. B.	Before operation—	plus 56%	172/ 78	120	77
	After operation—	minus 10%		108	98
	Myxedema Before and After Administration of Thyroid Extract				
M. W.	Before thyroid—	34%	140/ 90	64	96
	After thyroid—	1%	136/ 94	80	80
G. H.	Before thyroid—	48%	110/ 80	44	52
	After thyroid—	26%	110/ 76	72	72

study the effect of elevating the metabolic rate on venous pressure. The results of reducing and elevating the basal metabolic rate on venous pressure, pulse rate, and arterial pressure are summarized in Table II.

RESULTS

In contrast to the previously quoted reports, our studies failed to reveal any significant deviations from the normal in venous pressure either in the thirteen cases of Basedow's syndrome with elevated basal metabolism or in the two patients with myxedema. Our results are within the usually accepted upper and lower limits of normal venous pressure. The five patients with Basedow's syndrome who were subsequently subjected to subtotal thyroidectomy showed a return to normal variations in basal metabolism after operation, the fall in metabolic rate varying from 30 to 66 per cent and yet in none of these patients was there a significant change in venous pressure from the level before operation. The slight changes which were found were well within the limits of experimental error and were inconstant in direction. The same lack of change was true in the cases of the two patients with myxedema, in one of whom the basal metabolic rate was elevated from –34 to –1 per cent and in the other, from –48 to –26 per cent by administration of thyroid extract.

It is peculiarly significant that even in the same patient no noteworthy changes in venous pressure occurred after such marked differences in basal metabolism as were produced by thyroidectomy in Basedow patients or by administration of thyroid extract in myxedema. It was also significant that no apparent relation existed between changes in pulse rate or blood pressure and venous pressure during such large variations in basal metabolism.

It is evident that in this series of patients neither an elevation nor a depression of basal metabolic rate was sufficient to cause significant changes in venous pressure. This was true whether the rise or fall in basal metabolic rate was due to disease or to therapeutic procedures. These results do not exclude the possibility that venous pressure may be altered by changes in basal metabolic rate under certain experimental conditions. One may conclude, however, that the degree of change occurring under the conditions in this study was not of sufficient magnitude to be reflected in the form of significant variations in venous pressure even though the changes in basal metabolic rate were striking.

SUMMARY

1. Venous pressure was found to be normal in a series of thirteen patients with Basedow's syndrome and an elevated basal metabolism.

and in two patients with myxedema and a subnormal metabolic rate. None of the fifteen patients presented evidence of cardiac embarrassment.

2. These findings are in contrast with those previously reported in the literature. It is possible that cardiac failure or variations in experimental technic affected the results previously reported.

3. This study is of significance because no definite change in venous pressure occurred in the *same* patient when the basal metabolic rate was markedly reduced by thyroidectomy in those with Basedow's syndrome or by an elevation in metabolic rate by administration of thyroid extract in myxedema.

4. The degree of change in metabolism, pulse rate and blood pressure was apparently of insufficient magnitude in this series of patients to be reflected as important variations in venous pressure.

We are indebted to Dr. S. G. Taylor of the Medical Department of the Cook County Hospital for the patients used in this study.

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Department of Clinical Reports

LONG CONTINUED VENTRICULAR TACHYCARDIA

Report of an Unusual Case*

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ISOLATED premature ventricular contractions form, with the exception of sinus arrhythmia, the most common irregularity of the heart beat recorded graphically. Paroxysms, or runs of ventricular premature beats constituting ventricular tachycardia, are on the contrary of rare occurrence. The first case with electrocardiographic studies was reported by Lewis[1] in 1909. Strauss[2] in 1930 in a painstaking review of the subject collected 63 cases possessing what he considered adequate diagnostic criteria. To these he added two cases of his own, bringing the total to 65 properly attested cases. Roger Froment[3] devotes a monograph of 501 pages to this subject. Although tracings are not reproduced in all instances, it seems likely that 66 of his 99 collected cases would meet the requirements strictly necessary for proper identification. Froment's work and that of Strauss are in close agreement. Strauss' study of the age incidence disclosed the fact that 26 per cent of the cases occurred in individuals of over sixty years, 60 per cent between fifty and sixty years, and 14 per cent before fifty years of age. Three cases only were recorded in individuals under the age of thirty years. Paroxysmal ventricular tachycardia has usually been observed to occur in association with some established cardiac disease. In a very much smaller percentage of recorded cases it has appeared to be spontaneous—without laboratory or clinical evidence to throw light on its etiology. Among Strauss' 65 collected cases 11 were of this type. The condition is sufficiently uncommon to warrant the reporting of isolated instances, especially if they be of this cryptic type.

This report deals with the clinical and electrocardiographic studies of a patient who developed, at the age of nineteen years, paroxysms of ventricular tachycardia which persisted with increasing frequency and growing duration until her eventual death, approximately nine months after their first appearance. We were able to observe five separate paroxysms varying in duration from thirty-seven hours to thirty-two days. The case is of interest because of the youth of the patient, the

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absence of all other signs of heart disease, and the unprecedented duration of the paroxysms.

CASE REPORT

Hospital No. 275,953. American-born Hebrew girl, aged nineteen years, was admitted to St. Luke's Hospital July 7, 1931, complaining of shortness of breath and attacks of palpitation of the heart of six months' duration; nausea and vomiting were often associated with these paroxysms. There had been some edema of the feet for one week. The patient had but very recently been graduated from one of our state universities, where she had proved herself to be a remarkable student, having made Phi Beta Kappa in three years. Previous to going to college she had always been well. Her mother affirmed that the girl had never had a serious illness, in particular denying the occurrence of chorea, arthritis, heart disease, or other significant infection. Patient's tonsils had been removed at the age of ten years. She was very obese. Her body weight at time of hospital entry was 225 pounds. At the age of seventeen years and during her sophomore year at college, having become extremely sensitive over her obesity, she joined a research diet squad, living on rations which approximated 1,000 calories daily. She remained on this regimen for four months, losing seventy pounds in body weight. Her physical efficiency suffered considerably as a consequence of this rapid reduction, and she was compelled to return to more liberal fare. During her senior year in college, her body weight at the time being considerably over 200 pounds, she returned to a strict reduction diet as nearly duplicating her earlier efforts in that direction as she could, her declared object being to reduce her weight to 150 pounds before graduation. She presently began to experience shortness of breath and periods of rapid heart action, sometimes with nausea and vomiting. This was about Christmas, 1930. For a number of weeks at the outset these manifestations were infrequent and transient, subsiding spontaneously. As spring approached, they became more frequent, severe, and prolonged; and she sought medical advice. The medication first administered was digitalis. This failed either to prevent or to shorten the attacks appreciably, and during April her physician administered quinidine.

This proved more effective, ameliorating the severity of her symptoms sufficiently to enable her to continue her college work until graduation. Shortly thereafter (May, 1931) she experienced an unusually severe attack and was admitted to the Michael Reese Hospital, where she remained ten days. Upon discharge from hospital observation her medication consisted of quinidine, rest in bed, and ice bag to precordium. Despite faithful adherence to this regime, attacks of palpitation continued to occur, averaging in duration from seven to ten days. The heart rate during attacks varied from 180 to 210. At times she vomited and was always extremely restless and unable to sleep. A particularly severe and prolonged attack of rapid heart action led to the development of swelling of her feet, and it was alarm over this manifestation that brought her to the hospital July 7. The patient's mother stated that during the month of June there had been administered 72 grains of digitalis besides more or less (unestimated) quinidine. Since the beginning of the attack the pulse had varied around 200.

Physical examination July 7, 1931. The patient was seen to be an unusually large and very obese girl, orthopneic and cyanotic. The heart rate was regular, 184 per minute counted with the stethoscope. No murmurs could be detected. The soft tissues of the feet and legs were the seat of pitting edema. The liver was enlarged two fingerbreadths and was somewhat tender to pressure. There seemed

to be a good deal of moisture at both lung bases. Signs of free fluid in thoracic and abdominal cavities were lacking. Great difficulty was encountered in properly adjusting the blood pressure cuff to the patient's fat arm. She complained greatly of the pressure from inflation of the cuff and resisted the procedure in a childish manner, so that no satisfactory blood pressure reading was ever secured. The urine analysis was reported as practically negative. The blood count was: red cells 4,865,000; leucocytes 12,500; hemoglobin 97 per cent or 21.83 gm. per 100 c.c. The blood chemistry proved practically normal. After ten days' incubation, blood culture was reported sterile. The two-meter x-ray film revealed a slight amount of fluid in the right thoracic cavity and a moderate increase in the transverse measurement of the heart.

Subsequent History.—To relieve her difficult breathing and mediate the cyanosis, oxygen was administered with much apparent benefit. The patient complained bitterly of pain in the neck which we interpreted as perhaps due to the constant forceful pounding of the great vessels of the neck. On the fourth day the heart rate suddenly slipped to 88, with a regular rhythm, the heart sounds being weak and indistinct. Her sensory discomforts quickly subsided, and there was some improvement in the edema. This remission which began on July 11 continued until 4:30 P.M. July 15 when the rate suddenly went to 200, with nausea and vomiting. This recurrence of the tachycardia was preceded by an emotional upheaval due to a disturbing family conference. After forty-eight hours of tachycardia the rate slowed to 120 with occasional premature contractions. On the following day the pulse was very irregular, heart rate 96, radial pulse 76. Free fluid was now demonstrable in the abdomen. There had developed a trophic ulcer over the sacrum. The body temperature varied from subnormal to 100° F. After forty-eight hours of moderate rate the heart action suddenly became again extremely rapid, with frequent skips. This paroxysm, during which the heart rate varied from 170 to 210, continued without observed intermission for eighteen days. During this exhausting paroxysm the edema greatly increased and fluid accumulated considerably in abdomen and right pleural sac. Acid base diuretics with salyrgan proved ineffectual in influencing this anasarca. Drainage of the legs with Southey's tubes was attempted but could not be continued owing to the objection of the patient. The liver became greatly enlarged and tender. All efforts at therapeutic control proved ineffectual. Quinidine by mouth and intravenously exerted no apparent influence. After eighteen days' continuous tachycardia the heart rate declined to 120 and subsequently to 92. An electrocardiogram made during this remission showed a rate of 102, sinus rhythm. This period of normal control continued for four days, and on occasion during this interval the heart was observed to be grossly irregular for short periods. After this brief improvement ventricular tachycardia again began and continued without observed interruption until death, a total of thirty-two days. Multiple decubital ulcers developed. Large hemorrhagic blisters which began as purpuric areas formed on the lower extremities. The patient died in terminal coma apparently from exhaustion. Consent for necropsy could not be secured.

During the period of our observation there occurred five paroxysms of ventricular tachycardia. The attacks persisted for four days; thirty-seven hours; eighteen days; four days; and thirty-two days, making in all a total of fifty-nine and one-half days.

ELECTROCARDIOGRAPHIC STUDIES AND DISCUSSION

Four tracings are presented, in at least two of which the diagnosis of paroxysmal ventricular tachycardia appears to be clearly established. A third tracing showing normal sinus rhythm during interparoxysmal

intervals is also presented. A fourth record is added differing in some details from all preceding ones, difficult to interpret beyond argument. An exactly similar tracing has never before been observed in our laboratory, nor does a fairly comprehensive search of available literature reveal one with identical characteristics.

Fig. 1 is a tracing made July 9, thirty-six hours after patient was admitted to the service. It shows paroxysmal ventricular tachycardia with complete dissociation, ventricular rate being 174 while auricular rate was 90. P-waves are upright in all leads; auricular cycle length 0.66; QRS notched and extremely aberrant; QRS cycle length 0.38; T_1 almost isoelectric; T_2 and T_3 cannot be identified.

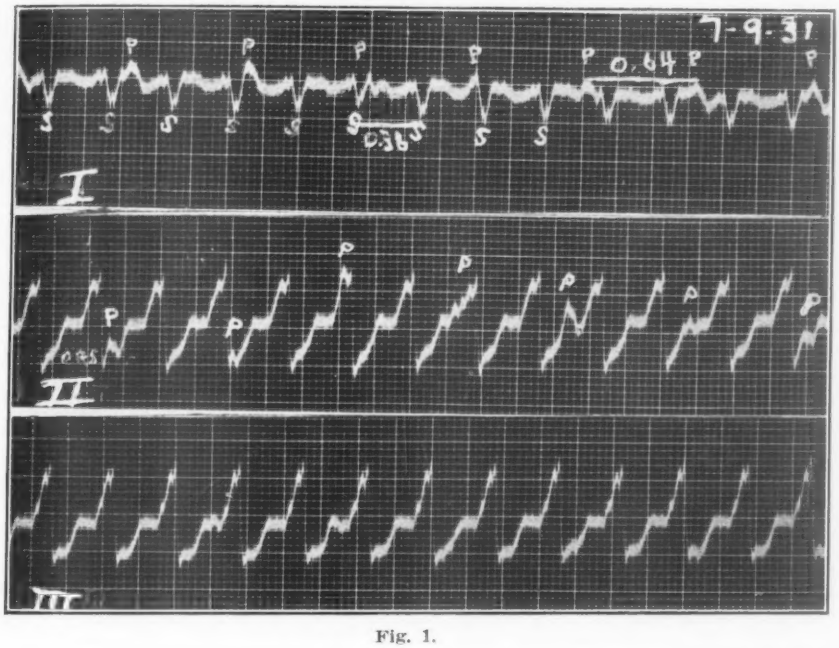

Fig. 1.

Fig. 2 is a record made July 31, three weeks after the tracing in Fig. 1, and during this interval normal sinus rhythm had prevailed for seventeen days. It is identical in all particulars with preceding curve except that QRS complex is upright in Lead I.

Fig. 3, August 5. Normal sinus rhythm. Heart rate 102. P-wave upright in Leads I and II with notching in Lead II. P-wave almost isoelectric in Lead III, T_1 and T_2 depressed. QRS complex shows low amplitude in all leads together with notching and slurring. One ectopic contraction of ventricular origin occurs in Lead III.

The final identification of the character of a paroxysm of tachycardia may be said to rest absolutely with the electrocardiogram. This is often

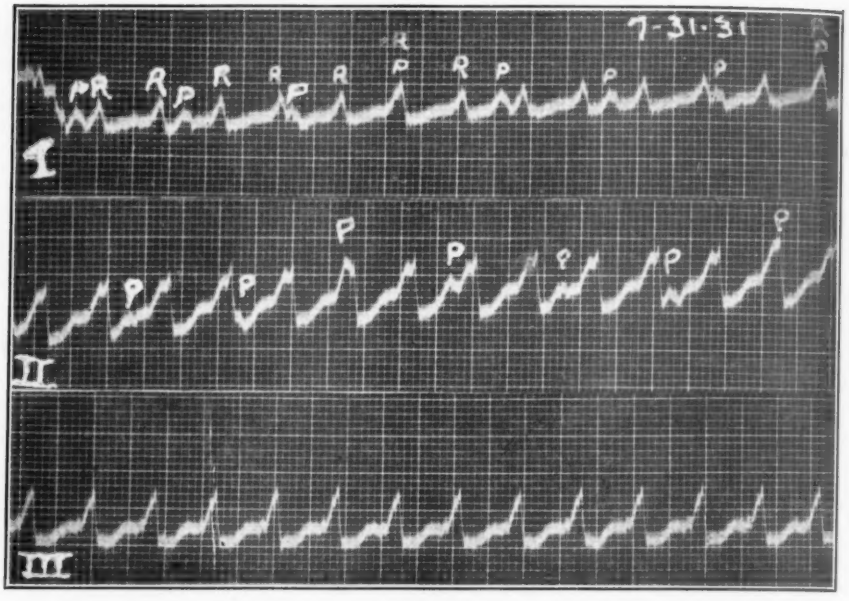

Fig. 2.

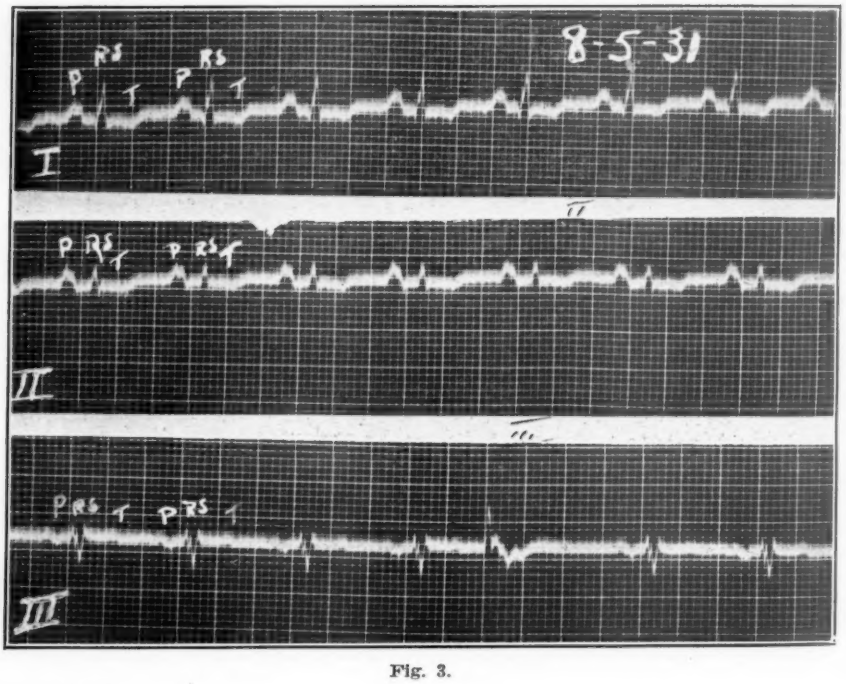

Fig. 3.

attended by considerable difficulty owing to variations and restrictions that have nullified many instances that were placed on record as ventricular tachycardia. If accuracy be observed in enforcing certain

criteria now generally recognized and acknowledged[4] paroxysmal ventricular tachycardia becomes a disorder that is rarely encountered.

Reference to the electrocardiograms here presented will admit no doubt of the diagnosis in tracings 1 and 2.

Fig. 4, August 19. This tracing presents a different problem. While the diagnosis of paroxysmal ventricular tachycardia seems fairly obvious, the mechanism is quite different from that exhibited in the preceding

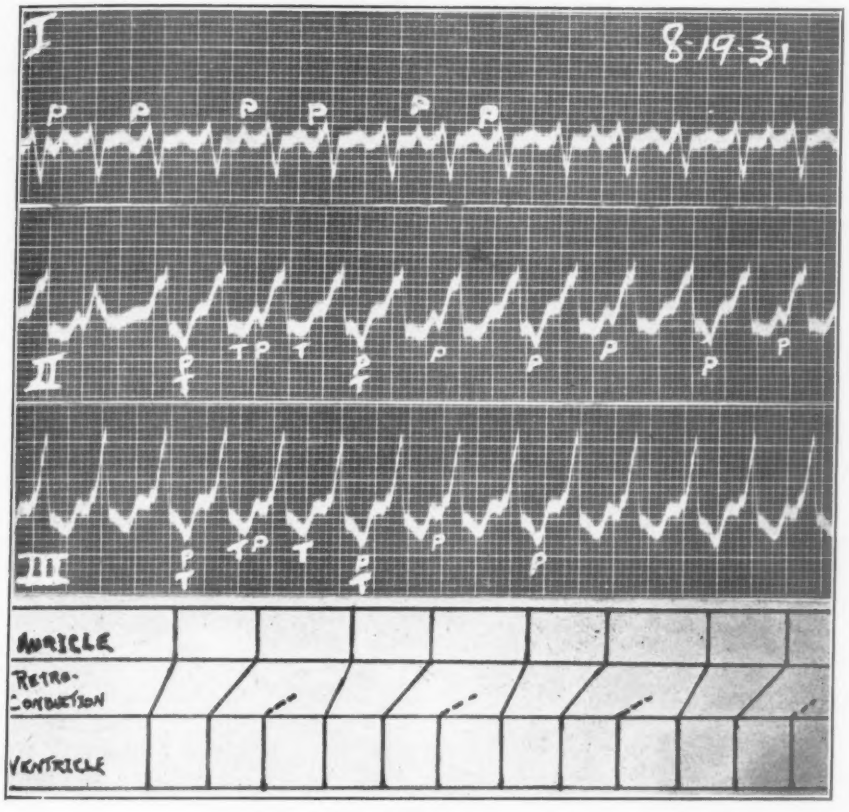

Fig. 4.

tracings. Two alternative interpretations are offered, neither one of which is entirely satisfactory.

1. Paroxysmal ventricular tachycardia with retrograde conduction and ventriculo-auricular block. This interpretation assumes that the pacemaker of the heart lies in the ventricle, and the auricle is activated by impulses travelling upward from the ventricle. The rhythm consists of a series of triads in which the first ventricular impulse provokes a prompt auricular response; the second ventricular impulse provokes a delayed auricular response; and the third ventricular impulse fails entirely to activate the auricle. This is the reverse of the Wenckebach type

of A-V block. Such an interpretation might well explain the events occurring in Leads II and III, but in Lead I it would assume that the first retrograde P-wave of each triad is upright, while the second is inverted. This assumption is not entirely satisfactory. If the first triad of Lead I be closely examined, it will be seen that both P-waves are inverted. It is this interpretation that has been illustrated in the tracing shown above.

2. Somewhat less satisfactory is the interpretation that tracing 4 represents paroxysmal ventricular tachycardia with complete dissociation between auricles and ventricles and a bigeminal auricular mechanism with alternate auricular impulses arising from different sources. Such a reading might be borne out by the auricular complexes themselves, but it presupposes a time relationship between the dissociated auricle and ventricle that could be brought about only by a very strange and perhaps unlikely coincidence.

SUMMARY

There is reported herewith an inveterate and fatal instance of paroxysmal ventricular tachycardia occurring in a girl of nineteen years without any other discoverable evidence of cardiac disease. The paroxysms were of unprecedented duration. The terminal paroxysm ending in death from cardiac exhaustion endured continuously for thirty-two days.

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ACUTE DIFFUSE MYOCARDITIS FOLLOWING EXFOLIATIVE DERMATITIS

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REFERENCES to acute diffuse myocarditis have appeared in medical literature since 1896. Various authors have utilized the terms acute interstitial myocarditis, acute myocarditis, acute isolated myocarditis, and Fiedler's myocarditis. The clinical pictures presented in the various reports vary too widely to consider it a clinical entity. The terminology must, therefore, depend on the pathologist.

In 1929 Scott and Saphir[1] found 36 reported cases in the literature and added two more. In 1931 Bailey and Andersen,[2] in adding one more, dispute the inclusion of three of the cases. This is mentioned to establish the relative rarity of the condition. A review of the above works will readily justify the inclusion of this case. In no instance has exfoliative dermatitis been listed as an etiological factor.

CASE REPORT

A. F., a Norwegian laborer, aged forty-two years, was admitted to St. Mary's Hospital on the Dermatology Service of Dr. George Doyle on August 13, 1931. The patient complained of malaise and itching all over the body. The skin of the entire body was red and edematous. It was a generalized dermatitis in the pre-exfoliative stage.

A search into the man's past brought out the following history of syphilis. About twenty years before he had had an initial lesion. A small but undetermined amount of treatment was given at that time. In September, 1930, a routine employment examination brought to light a strongly positive blood Wassermann reaction. At this time he received one bismuth and one neoarsphenamine injection. He was not seen again until July, 1931, when in seeking employment his record again brought him under treatment. He sought no symptom relief and complained of no illness. He was given three injections of bismuth and five neoarsphenamine injections of 0.3 gm. each. The first four injections were without untoward effect, but on the day following the fifth injection the skin itched and became red. This continued to increase in intensity, and two days later he was admitted for hospital care. Five injections of sodium thiosulphate and local treatment failed to check the advance in severity.

On August 24, eleven days after admission, he became dyspneic, the heart tones were weak, and the pulse was difficult to palpate. He improved under the use of stimulants and the oxygen tent.

On August 25 the skin was more edematous, and the crusting exudate of the exfoliative process was more pronounced. He was bringing up a frothy purulent material on coughing. Coarse moist râles were noted in the right upper lung field, and there was diminished resonance below. Temperature was 99° and respirations were 36.

On August 26 I made my first examination. He was lying flat in bed and appeared very ill. The skin of the entire body was covered by a scaly crust. Breathing was too labored to justify much questioning. He complained of feeling very sick, of an intolerable itching all over the body (which necessitated bandaging to keep him from scratching), and of difficulty in getting enough air. On physical examination the left lung seemed practically clear, but the right lung showed an extensive congestion with no demonstrable consolidation. A flat film of the chest taken in bed showed the above plus a questionable small area of bronchopneumonia in the left base. The heart outline was of the hypertensive type. Diathermy was applied to the chest, the oxygen tent was used and 10 c.c. of solution of digitalis were given intramuscularly during the course of the day.

On August 28 the patient felt better. The skin was unchanged, and the cough

Fig. 1.—Low power.

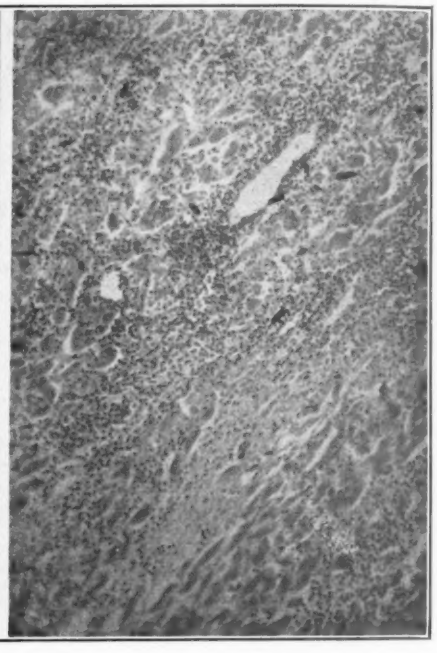

Fig. 2.—High power.

was easier and productive of a thick sputum. Six c.c. of digitalis were administered intramuscularly.

On August 30 the patient was weaker. The lungs were clearer, and coarse moist râles were heard over both bases. (It must be remembered that the dermatitis made auscultation difficult.) No consolidation was clinically demonstrable.

On August 31 the patient died suddenly. Owing to delay in locating relatives for purposes of securing permission, the autopsy was performed on the embalmed body under unfavorable conditions. The following positive findings were taken from the notes of the pathologist, Dr. G. L. Berdez.

The skin was red, desquamated and scaly with a serous exudate and a general edema. Multiple hemorrhagic infarcts were present in both lungs. There were 200 c.c. of fluid in the left pleural cavity and 150 c.c. in the right. The spleen was congested and there was cloudy swelling of both kidneys.

The heart weighed 720 grams and showed a diffuse myocarditis. There were no mural thrombi. There were some yellowish atheromatous plaques in the aorta, not extending into the coronary orifices or onto the aortic valves. The lumen of the coronary arteries showed not more than a Grade I narrowing at any point along the main branches. Cut sections showed a yellowish muscle of rather flabby consistency with grayish yellow mottling. The accompanying photomicrographs show a diffuse interstitial infiltration, mostly with lymphocytic and other mononucleated cells (Fig. 1). In Fig. 2 in the higher magnification, in addition to the above, polymorphonuclear cells are also numerous. There is a moderate amount of cloudy swelling and actual destruction of muscle fibers. No bacteria are noted.

DISCUSSION

In the recorded cases the most frequent clinical notations are substernal pain or oppression, congestive heart failure and sudden death. What chest pain this man had was ascribed to the rapidly appearing pulmonary congestion and the possible bronchopneumonia. The congestive heart failure was rather acute in onset eleven days after admission. Sudden death might have occurred at that time if emergency measures had not been available.

The commonest description of the heart muscle is that of grayish yellow mottled streaks on a background of dark red muscles of flabby consistency. This varies from plain dark red to streaked yellow and sometimes grayish red. This case showed the yellowish color of cloudy swelling.

The heart weighed 720 grams. This is higher than any figure given in previous reports. The flat plate of the lungs showed what was interpreted as a hypertensive outline. We are without benefit of blood pressure readings due largely to the severe dermatitis. At the age of forty-two years it is improbable that a great degree of long standing hypertension could account for much of this. No aortic insufficiency was noted. It therefore is reasonable to suppose that the bulk of the cardiomegaly, at least, was due to inflammatory changes in the myocardium.

Four main possible causes must be weighed: first, the syphilis itself; second, the direct action of the arsenic; third, the bronchopneumonia; and fourth, the exfoliative dermatitis with its associated infection or toxemia.

Since Warthin's original work,[3] much has been said regarding acute myocardial failure occurring in cases of latent syphilitic myocarditis. In these cases demonstration of the *Spirocheta pallida* has usually been possible in isolated areas, though diffuse cases have been reported. In the many sections studied in this case no spirochetes were demonstrated.

The direct action of the arsenic is certainly open to conjecture. Obviously there was a low tolerance or idiosyncrasy to the drug. It does seem, however, that a direct reaction would have occurred more rapidly in the form of cardiac embarrassment. It is presumed that the

direct action is in the nature of a dramatic allergic phenomenon and that as such it would more nearly approximate the chronological onset of the skin manifestations.

The autopsy findings ruled out a direct infection from bronchopneumonia, for what was thought to be bronchopneumonia turned out to be an area of infarction.

Lastly comes the question of the exfoliative dermatitis. The literature and the experience of those men who were kind enough to discuss this case offer no precedent. The expedient of exclusion leaves the dermatitis as the most probable cause of the myocarditis. The absence of bacteria suggests the toxic rather than the infectious nature.

SUMMARY

1. A case is reported in which a pathological diagnosis of acute diffuse myocarditis was made.

2. A brief comparison with the most constant findings in other cases is made.

3. Exfoliative dermatitis is believed to be the direct cause.

A case is reported of late, latent syphilis in which treatment by arsenic was followed by exfoliative dermatitis. During this attack severe cardiac symptoms appeared and progressed rapidly to a fatal issue. The lesions of acute diffuse myocarditis were found at autopsy.

The exfoliative dermatitis is believed to have been the cause of the myocardial changes.

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Department of Reviews and Abstracts

Selected Abstracts

Waring, James J., and Black, W. C.: The Syndrome of Obstruction in the Lesser Circulation. Am. J. M. Sc. **187:** 652, 1934.

This survey of the symptoms of obstruction in the lesser circulation has been undertaken to emphasize the too frequently forgotten importance of the integrity of the pulmonary circulation in the process of oxygenization.

The clinical evidences of chronic anoxemia are commonly dyspnea, cyanosis, and polycythemia, rarely precordial pain and syncope. Signs of slowly developing strain upon the right side of the heart in the absence of other obvious cause, such as valvular defects, suggest obstruction in the lesser circulation. Whether the obstruction be in the capillaries, as in certain instances of so-called Ayerza's disease, or in the arterioles and small arteries or whether the obstruction be in the larger divisions of the pulmonary arteries, the underlying clinical picture of chronic anoxemia and failure of the right side of the heart is essentially the same.

Primarily obstructive lesions of the pulmonary circulation which involve extensively the pulmonary capillaries or pulmonary arteries and are not immediately fatal raise the pulmonary arterial pressure and produce hypertrophy of the right ventricle and also interfere with respiratory function and produce anoxemia.

Horton, Bayard T.: Arteriovenous Fistula Involving the Common Femoral Artery Identified by Arteriography. Am. J. M. Sc. **187:** 649, 1934.

This case report serves to illustrate the importance of definitely determining the site of an arteriovenous fistula by means of arteriography and to demonstrate the clinical signs and symptoms of acquired arteriovenous fistula. With the history, the presence of a bruit, the thrill over the right thigh and the bradycardiac reaction, the diagnosis of arteriovenous fistula of the acquired type seemed definitely established. The diagnosis was confirmed by the demonstration of a high admixture of arterial and venous blood in the right femoral vein. The site of the fistula could be determined only by means of arteriography or by surgical exploration.

Griffith, George C., Chamberlain, Charles T., and Kitchell, J. Roderick: Observation on the Practical Significance of Venous Pressure in Health and Disease With a Review of the Literature. Am. J. M. Sc. **187:** 642, 1934.

In this article the authors discuss the clinical application of determinations of venous pressure and the usefulness of the procedure in the hands of the general practitioner who is confronted with diagnostic problems of cardiovascular disease. There is a brief discussion of the normal venous pressure and its physiologic variations. Four fundamental functional factors affecting peripheral

venous pressure namely: (1) vis a tergo or heart action; (2) intrathoracic pressure; (3) hydrostatic level; (4) volume of blood in the vein are discussed.

Use of venous pressure determinations in various clinical conditions is discussed. It is pointed out in particular that in primary congestive heart failure and in other disease entities complicated by or simulating cardiac decompensation, the procedure should offer practical diagnostic, prognostic, and therapeutic aid. The significance of venous hypotension is discussed.

Goldbloom, A. Allen: Clinical Evaluation of Lead IV (Chest Leads). Am. J. M. Sc. **187:** 489, 1934.

The purpose of this study was to see whether Lead IV would be positive only in those cases where the routine three leads were positive or whether it might sometimes be positive while the routine three leads were negative. If the fourth lead were positive only in conjunction with positive routine three leads, it would be superfluous as an additional method; but, if it should prove positive in any case where the routine three leads were negative or doubtful, it would be of definite value. All the 86 patients were ambulatory except 13. Forty of the 86 patients had definite clinical symptoms of coronary artery disease with or without a history of acute occlusion. The method carried out in this series was that of Wolferth and Wood; although in a few cases posteroanterior position was also used and proved of value.

Of these cases with coronary artery disease, 28 showed positive routine 3 leads, 12 showed an abnormality in Lead IV and positive routine 3 leads, and 3 showed an abnormality only in Lead IV. Four of the 13 cases of acute coronary thrombosis showed an abnormal Lead IV, whereas the routine 3 leads were negative.

A serial study of a case of coronary thrombosis showed that abnormal Lead IV may persist long after abnormal changes have disappeared from routine 3 leads. Since abnormal Lead IV proves positive in cases of coronary artery disease and acute coronary thrombosis, its employment as a routine electrocardiographic method is advocated.

Schwartz, Sidney P., and Jezer, Abraham: Studies on Transient Ventricular Fibrillation. I. Observations on the Alterations in the Rhythm of the Heart Preceding Syncopal Seizures in a Patient With Normal Sinus Rhythm. Am. J. M. Sc. **187:** 469, 1934.

Clinical manifestations were correlated with electrocardiograms of the alterations in the rhythm of the heart of a boy with infectious myelitis during a period when he was experiencing recurrent syncopal attacks, each of several minutes' duration. Prior to such seizures, there was at first an acceleration of the basic sinus rate from an average of 90 to 150 beats per minute but the rhythm was regular. Sooner or later, in an unpredictable manner, premature ventricular beats began to disrupt the basic rhythm, first appearing after every fourth normal beat and then alternately after every other normal beat. To these premature beats there were added from time to time recurrent groups of aberrant ventricular oscillations, only the first two or three which could be heard at the apical region of the heart or felt at the pulse, thus resulting in periodic irregular "pulse pauses." When the duration of these "pulse pauses" was only eight or ten seconds, there was momentary loss of consciousness with pallor of the skin. If they lasted between twenty and forty seconds, there was loss of consciousness. If they were of a duration longer than forty seconds, there resulted a typical Stokes-Adams seizure with loss of consciousness, epileptiform convulsions, incon-

tinence of feces and urine and stertorous breathing ending in apnea with intense cyanosis.

These recurrent periods of aberrant ventricular oscillations are short runs of ventricular fibrillation, and their presence in the electrocardiographic tracings was the most characteristic feature of the alterations in the rhythm of the heart that preceded syncopal seizures in this patient.

Schwartz, Sidney P., and Hauswirth, Louis: Studies on Transient Ventricular Fibrillation. II. Observations on the Alterations in the Rhythm of the Heart Preceding Syncopal Seizures in a Woman With Transient Auriculoventricular Dissociation. Am. J. M. Sc. **187**: 478, 1934.

Successive electrocardiograms were correlated with the clinical manifestations of a woman who was suffering from recurrent syncopal seizures. Particular attention was paid to the alterations in the rhythm of the heart that preceded syncope.

The patient usually showed normal sinus rhythm in between attacks. For some time prior to a seizure, the normal sinus rhythm alternated with that of auriculoventricular dissociation. There was a marked waxing and waning of the rates of both the auricles and the ventricles during the presence of auriculoventricular dissociation.

Sooner or later this dissociated rhythm would be interrupted by premature ventricular beats coming on singly so as to form a bigeminal rhythm. Occasionally a normal sinus beat would be interpolated in this dissociated rhythm, appearing at first after every eighth effectual ventricular contraction and then more frequently. Alterations between the normal sinus rhythm and the dissociated rhythm resulted in grouped beats forming trigeminies and quadrigeminies with regular periodicity.

When the appearance of these various rhythms had materially increased the rate of the ventricles after they had been slowed during auriculoventricular dissociation, recurrent ventricular oscillations began further to disrupt the cardiac mechanism. These aberrant ventricular oscillations were variable in shape, size, and form from beat to beat. They were associated clinically with ineffectual ventricular contractions resulting in periodic "pulse pauses," absent heart sounds, and a collapse of the circulation.

If these ventricular oscillations lasted from eight to ten seconds, then the patient merely shut her eyes, and her face assumed an ashen gray pallor. If they were of twenty seconds' duration, she lost consciousness. If they lasted longer than forty seconds, a typical Stokes-Adams seizure ensued.

These short groups of ventricular oscillations are short runs of ventricular fibrillation, and no syncopal seizure resulting from ventricular fibrillation appeared without these shorter runs heralding a major attack. Because of this, they are pathognomonic for ventricular fibrillation, and their recurrent presence in any electrocardiogram should help in the diagnosis of the cardiac mechanism underlying such syncopal seizures.

Seecof, David P., Linegar, Charles R., and Myers, Victor C.: The Difference in Creatine Concentration of the Left and Right Ventricular Cardiac Muscles. Arch. Int. Med. **53**: 561, 574.

Studies have been made on the creatine content of the right and left ventricular muscle on 114 human and 9 animal hearts. The method employed for the creatine determination is a modification of that of Rose, Helmer and Chanutin. It was found that the concentrations of creatine of the left and right ventricular muscles of the heart are different, the former having the greater concentration.

Attention has also been called to correlations between creatine content and age and weight of the heart. From the standpoint of creatine and creatinine metabolism, it is significant that when the creatine content of voluntary muscle exceeds about 400 mg. (the probable saturation point) a corresponding elevation in the cardiac muscle also occurs, and further, that the retention of creatinine in renal disease has an augmenting influence on the creatine content of both cardiac and voluntary muscle.

In addition to embryological, anatomical, physiological and pathological observations, chemical evidence is now presented pointing to the fact that the left and right ventricles are different muscles. These differences justify the concept that the heart is not a uniform muscle but that it is made up of several qualitatively different muscles. The significance and possible practical value of this concept are discussed.

Harrison, W. G., Calhoun, J. A., and Harrison, T. R.: Congestive Heart Failure. XVIII. Clinical Types of Nocturnal Dyspnea. Arch. Int. Med. 53: 561, 1934.

A clinical study has been made of thirty patients who had cardiac disease and who suffered from attacks of nocturnal dyspnea. Most of the subjects were more than forty years of age. The chief causes of cardiac disease in these cases were hypertension, arteriosclerosis, and syphilitic aortic insufficiency. There were only two patients with rheumatic heart disease, and of these only one had uncomplicated mitral stenosis. The occurrence of nocturnal dyspnea is restricted almost entirely to patients with disorders which cause a strain on the left ventricle. Uncomplicated syphilitic aortitis (i.e., without aortic insufficiency, occlusion of the coronary vessels or aneurysm) practically never causes nocturnal dyspnea.

Cardiac enlargement and diminished vital capacity were constant objective findings; premature beats and gallop rhythm occurred in a large number of the patients. Only four patients in the series had auricular fibrillation.

The following factors have been found to be precipitating and predisposing causes of the attacks: (1) the position of the body in twenty-seven cases, (2) cough in twenty-three cases, (3) the amount of activity engaged in during the preceding day in twenty-one cases, (4) abdominal distention in seventeen cases, (5) large evening meals in twelve cases, (6) constipation and desire for bowel movement in twelve cases, (7) hunger in eight cases, (8) unpleasant dreams in eight cases, (9) heat in eight cases, and (10) urination in seven cases.

Analysis of the histories of the cases indicates that nocturnal dyspnea may be subdivided into several types of respiratory distress:

1. A type which is not paroxysmal but which develops gradually during the course of the day, usually appearing first in the late afternoon and reaching its maximum intensity at bedtime. For this syndrome the name "evening dyspnea" is proposed.

2. Attacks of shortness of breath appearing only at the onset of sleep and tending to prevent the patient from reaching a state of deep sleep. However, if such a patient falls into a sound sleep, he is likely to remain free from attacks throughout the remainder of the night. Patients with this type of dyspnea frequently exhibit Cheyne-Stokes respiration and are unlikely to have seizures of acute pulmonary edema.

3. Attacks of dyspnea which begin after the patient has begun to sleep soundly and which are likely to cause acute edema of the lungs. Cheyne-Stokes respiration is an infrequent finding in patients with this type of dyspnea.

4. Combination forms. The same patient may have all three types of dyspnea or any two of them.

In subsequent articles objective observations will be presented concerning these various forms of respiratory distress.

Parker, Frederic, Jr., Keefer, Chester S., Myers, Walter K., and Irwin, Ralph L.: Histologic Changes in the Knee Joint With Advancing Age. Arch. Path. 17: 516, 1934.

Histological examination of the tissues from 100 knee joints of patients who had died of miscellaneous diseases was made. The gross anatomical changes have been reported in a previous article. The examination revealed the following observations: The synovia was essentially normal except in cases in which there were alterations in the cartilage. In these the capsule was somewhat thickened, papillary projections of the synovia occurred, and occasionally there were small collections of lymphocytes about the blood vessels. The cartilage showed fibrillation, degeneration, and some areas of regeneration. In some cases it was completely destroyed.

The subchondral bone was thickened owing either to compression or to formation of new bone. The marrow spaces were frequently filled with fibrous tissue, cysts, and areas of cartilage. Bony projections or so-called exostoses were due to a projection of bone and cartilage over the edge of the joint surface or to a depression of the cartilage below its original level, thus giving the appearance of bony overgrowth. They resulted from a forcing outward of bone and cartilage by flattening of the joint surface owing to pressure and erosion.

These changes are identical with those previously described as characteristic of degenerative arthritis. The evidence is that they are the result of injury and repair and that they occur with increasing frequency with advancing age.

Gilchrist, A. Rae: Ephedrine Sulphate and Barium Chloride in the Prevention of Stokes-Adams Seizures. Brit. M. J. 1: 610, 1934.

In six cases of complete heart-block ephedrine taken orally increased the rate of ventricular beating in four. In two patients the test was indecisive. Barium chloride produced no demonstrable effect on the ventricular rate in the four cases responding to ephedrine. It did no harm in doses larger than those originally recommended.

In two cases of complete heart-block complicated by occasional Stokes-Adams seizures, ephedrine taken for two and one-half and one and one-half years respectively proved entirely successful in the prevention of syncopal attacks. When the drug was discontinued, typical seizures returned.

It is recommended that the dose of ephedrine should be the minimum quantity consistent with an acceleration of the resting ventricular rate. Larger doses may cause overstimulation. If the drug be then suddenly omitted, profound slowing of the ventricular rate, with repeated Stokes-Adams attacks may occur as a result, presumably of exhaustion of the idioventricular center. A dose of one-half grain by mouth at eight-hour intervals may be sufficient. In the absence of positive findings, it is difficult to credit barium chloride with the power of preventing Stokes-Adams seizures.

Perry, C. Bruce: The Peripheral Circulation in Acute Lobar Pneumonia. Quart. J. Med. 3: 273, 1934.

In an attempt to provide definite evidence that the condition in pneumonia called heart failure is usually the direct sequel of failure at the periphery of the circulation rather than in the heart, a study of the failure of the small vessels

of the skin in patients with lobar pneumonia has been made. The reactions of the small vessels of the skin were studied in 26 cases of lobar pneumonia. Observations were made on the skin color, the blood pressure, the response of the skin vessels to histamine, to stroking and to adrenalin, and finally the back pressure on the circulation required to accelerate the blanching produced by the latter.

These reactions show an impaired efficiency in the contractility of the capillaries at the height of the disease. The recovery of the capillaries is slow and not immediately affected by the crisis. Part at least of the circulatory failure met with in lobar pneumonia is due to this impaired efficiency of the small blood vessels. The blood pressure is raised rather than lowered during the acute phase of the disease.

Bain, C. W. Curtis: Observations in the Speed of the Circulation. Quart. J. Med. 3: 237, 1934.

The time taken for the blood to travel from the arm to the face in normal subjects as shown by the histamine flush test is twenty-two seconds. The normal range is from nineteen to twenty-five seconds. The flush times are fast in hyperthyroidism, in the effort syndrome, in advanced anemia, and in diseases of the lung.

In the diseases of the heart some patients have had normal flush times; they have not been incommoded by their hearts. Others who have had no symptoms have had flush times from twenty-five to thirty seconds. These may be regarded as having a measure of cardiac insufficiency. Dyspnea and effort angina appear when the flush times have slowed to thirty-one seconds. It is suggested that dyspnea and effort angina should be regarded as alternative symptoms of cardiac failure.

Venous congestion is found in about half of those whose flush times are thirty-two seconds or more. The remainder include those suffering from anginal attacks and those who have been prevented from overexerting themselves. Edema is an almost constant finding in those whose flush times are forty-two seconds or more.

The above figures apply only when the lungs, blood, and basal metabolism are normal. When heart failure is complicated by pulmonary diseases, advanced anemia, or hyperthyroidism, the flush times are faster. Corresponding to the grade of failure, the heart will be less severely damaged than would be the case if these complications were absent, and great improvement may be expected if they can be removed.

Hirsch, I. Seth: The Recording of Cardiac Movements and Sounds by the Roentgen Ray (Kymophonoroentgenography). Radiology 22: 403, 1934.

The author describes a simple graphic method of obtaining a permanent record of the movements of the heart on a single film. Essentially this method is roentgenography through a slit diaphragm placed close to the object in motion, the recording film not being at rest as in ordinary roentgenography but moving at a constant rate of speed at right angles to the direction of the slit. The apparatus is of the multiple slit type. It consists of an impervious plate with slits of equal width, a mechanism for moving a film at a constant speed behind a grid, a mechanism for energizing the x-ray tube shortly after this movement begins and for cutting off the energization of the tube shortly before the film movement ends.

It is believed that this kymographic method contributes the following information to the morphological and physiological study of the heart: (1) the actual make-up of the cardiac shadow; (2) the shape of the heart as a whole, or any

of its chambers during the various phases of movement; (3) size of the heart in systole and diastole or any intermediate phase; (4) characteristics of the movement of the heart as a whole or of its various chambers; (5) activity and accomplishment of the cardiac muscle; (6) the relationship of contraction to conduction phenomena; and (7) the relationship of movement to sound phenomena.

Ayman, David: Heredity in Arteriolar Hypertension. Arch. Int. Med. 53: 792, 1934.

To determine more clearly the presence of a familial or hereditary factor in arteriolar (essential) hypertension, a direct study of the blood pressure, height, and weight of 1,524 members of 277 families was made.

It was found that in 780 members, aged from fourteen to thirty-nine years, of the second generation of the families, elevated systolic and diastolic blood pressure readings (140 systolic and 80 diastolic, or higher) occurred in 148 subjects. These 148 subjects had the same average age and sex incidence as the entire group of 780 children, but they were 14.3 pounds above the average weight compared to 4.5 pounds above the average weight for the normal children.

The families studied were then grouped according to the presence or absence of arteriolar (essential) hypertension in one or both parents. In the families whose parents had absolutely normal blood pressures, the incidence of elevated blood pressures in the children was only 3.1 per cent. In the families in which one parent had arteriolar hypertension, the incidence of elevated readings in the children rose to 28.3 per cent. In the families in which both parents had arteriolar hypertension the incidence of elevated readings in the children reached the striking level of 45.5 per cent.

Of 70 brothers and sisters of parents with normal blood pressures, 37.3 per cent had elevated blood pressure readings; whereas of 86 brothers and sisters with arteriolar hypertension, 65.3 per cent had elevated blood pressure readings.

Finally, 18 families, in which parts of three generations were available, were studied and results were found strikingly similar to those given in the preceding paragraph.

The results presented show that there is an unusually high incidence of elevated blood pressure readings in the children, brothers, sisters, and parents of subjects with arteriolar hypertension, as compared with similar relatives of subjects with normal blood pressure. These results are strong evidence for the existence of a hereditary factor in arteriolar (essential) hypertension.

Harrison, William Groce: Cerebrospinal Fluid Pressure and Venous Pressure in Cardiac Failure. Arch. Int. Med. 53: 782, 1934.

The cerebrospinal fluid pressure is markedly elevated in persons with congestive heart failure.

The cerebrospinal fluid pressure, except for slight variations, usually runs closely parallel to the venous pressure in the prone position in persons with cardiac failure; and, as a rule, the average ratio between the spinal fluid pressure and the venous pressure (1.6) in the patient with cardiac disease corresponds closely to that in the normal person. In general, either may be predicted from knowing the other.

The fall in cerebrospinal fluid pressure usually runs closely parallel with the fall in venous pressure as the patient with cardiac failure regains compensation.

Spinal drainage in patients with congestive heart failure was followed by a fall in venous pressure in eight instances, by a rise in two instances, and by no change in three instances. In the majority of cases spinal drainage was followed by a decrease in dyspnea.

The cisternal pressure is much less in patients in the sitting than in the prone position, although the systemic venous pressure and spinal fluid pressure are greater. This difference in cisternal pressure and hence in cerebral venous pressure is more pronounced in patients with cardiac failure; its bearing on orthopnea is discussed.

The relationship of the increased intracranial pressure to Cheyne-Stokes' respiration and hypertension in patients with congestive heart failure is discussed.

Lewis, J. K.: Nature and Significance of Heart Sounds and of Apex Impulses in Bundle-Branch Block. Arch. Int. Med. 53: 741, 1934.

The nature of the physical signs present in twenty patients with bundle-branch block and in three patients with "atypical" bundle-branch block has been determined by means of records of the heart sounds and apex cardiograms. Records of the heart sounds were obtained from all patients; apex cardiograms, from fourteen.

Physical signs of two distinct types occurred. Presystolic gallop rhythm was present in nine patients. In three of these patients a presystolic impulse was associated with the presystolic sound; in one the impulse was the only sign present.

A reduplicated first sound, entirely systolic, occurred in five patients. A double systolic impulse was present in one patient. A reduplicated first sound and a double systolic impulse were not found together in any of the patients studied.

The presystolic gallop rhythm present in these patients was the same as that found in persons without bundle-branch block except for a tendency for the interval between the P-wave and the gallop sound to be prolonged. The lengthening of this interval may be related to the absence of severe grades of circulatory failure in this particular group at the time of examination. The presence of gallop rhythm in bundle-branch block could be accounted for by the fact that both conditions occur in the same general type of heart disease and under the same circumstances. It could not be related to the bundle-branch block itself (or to asynchronism of the ventricles).

The incidence of gallop rhythm in the whole group was higher than that present in an unselected group of patients with degenerative heart disease. The explanation for this fact was not entirely clear, but the frequency of the anomaly appeared to be a reflection of the severity of the heart disease which accompanies bundle-branch block.

The frequency with which a reduplicated first sound occurred and its close association with the QRS complex suggest that it may be produced by asynchronism of the ventricles. However, evidence to prove or to disprove this point did not appear to be adequate.

The nature of the physical signs present was not such as to permit their use as diagnostic signs of bundle-branch block.

Harrison, W. G., Calhoun, J. A., Marsh, J. P., and Harrison, T. R.: Congestive Heart Failure. XIX. Reflex Stimulation of Respiration as the Cause of Evening Dyspnea. Arch. Int. Med. 53: 724, 1934.

A comparison has been made between morning and evening values of the gases in arterial blood and of respiratory and circulatory functions in a group of patients who had congestive heart failure and who suffered from dyspnea which was more marked in the evening than in the morning. The following results were obtained:

1. The oxygen capacity of the blood tended to be higher in the morning, and the oxygen saturation was usually greater in the evening. The differences were usually so slight as to be negligible.

2. Consistent variations were not observed in the hydrogen ion concentration, the carbon dioxide content or the carbon dioxide pressure of the blood. On an average the blood was slightly more alkaline in the evening and had slightly lower values for carbon dioxide content and carbon dioxide pressure.

3. No consistent alterations in heart rate or blood pressure were observed.

4. The consumption of oxygen was about 10 per cent higher in the evening than in the morning. The respiratory rate and minute ventilation were greater in the evening by an average of 15 per cent. The vital capacity was slightly lower in the evening in practically every instance, but the difference found was often not greater than the error of measurement.

5. Control observations were made on a group of patients without cardiac disease and on a group of patients with cardiac disease but without dyspnea. These two groups differed from the dyspneic subjects in the following results:

(a) Their diastolic blood pressures were usually lower in the evening than in the morning, whereas no change was observed in the patients with dyspnea.

(b) Although their increase in consumption of oxygen in the evening was of about the same degree, they exhibited no increase in respiratory rate and much smaller increases in ventilation. Likewise, the control group did not exhibit constant changes in vital capacity.

Experiments were performed on dogs in order to determine whether pulmonary congestion of such slight magnitude as to cause a barely measurable decrease in vital capacity could cause reflex stimulation of respiration. The following results were obtained:

1. In animals with intact vagus nerves the introduction of as little as 25 c.c. of blood into the left pulmonary artery (the left pulmonary veins being tied) led to a well-marked increase in respiratory rate and in ventilation.

2. Introduction of the same amount of air into the right pleural cavities of the same animals caused less marked and less sustained respiratory stimulation.

3. After bilateral vagotomy the introduction of blood or air produced no significant changes in respiration.

As a result of these clinical and experimental observations the following conclusions are drawn:

The pulmonary afferent fibers of the vagus nerve are extremely sensitive to pulmonary congestion. A very small amount of excess blood in the pulmonary vascular bed causes a well-marked reflex stimulation of breathing.

Evening dyspnea in patients with congestive heart failure is probably to be attributed to reflex respiratory stimulation and a decrease in vital capacity because of an increase in the degree of the preexisting pulmonary congestion. The greater congestion of the lungs in the evening than in the morning is believed to be due to greater bodily activity during the waking hours.

Katz, Louis N.; Soskin, Samuel; Schutz, William J.; Ackerman, Walter; and Plaut, Julian L.: A Metabolic Exercise Tolerance Test for Patients With Cardiac Disease. Arch. Int. Med. **53**: 710, 1934.

A relatively simple method has been devised for measuring the excess oxygen consumption in exercise, the oxygen debt, and the recovery time. This metabolic tolerance test has been applied to a group of normal persons and to a group of patients attending the clinic for cardiac disease, and the results have been compared.

It was found that these measurements, particularly of the excess oxygen consumption of exercise, were greater than normal in patients with organic heart disease and with a history of some limitation of activity, even when no congestive heart failure was present. When these patients were classified into subgroups, according to the history of the degree of limitation of activity, the

measurements become progressively greater as one passes from the group with no limitation of activity to the group with marked limitation.

It is concluded that this test, which yields an objective quantitation of the cardiac capacity of a patient at the time of examination, merits further consideration as an adjunct in the study of cardiac disease.

Soskin, Samuel; Katz, Louis N.; Markle, Philip; and Henner, Robert: The Metabolic Exercise Tolerance Test. Arch. Int. Med. **53**: 706, 1934.

A simplified method is described for determining the excess oxygen consumption during exercise and time required for recovery by the metabolic exercise tolerance test. The test is hardly more difficult to perform than the ordinary basal metabolism test and is suitable for routine use in the clinical laboratory. The objective nature of the test, which eliminates the subjective influence of both patient and physician, makes it particularly suitable for the accumulation of data by different observers on large groups of persons. Such an application might be made in the classification of cardiac disability for insurance purposes.

Eggleston, Cary: The Medical Treatment of the Thyrocardiac. Am. J. M. Sc. **187**: 737, 1934.

Four clinical types of thyrocardiac disease may be distinguished: first, those patients with Graves' disease with structurally normal hearts; second, Graves' disease in patients with rheumatic heart disease; third, thyrotoxicosis in patients with arteriosclerotic or hypertensive heart disease; and fourth, patients with "masked hyperthyroidism." Emphasis is laid upon thyrotoxicosis as the common factor primarily responsible for the cardiac manifestations in all four types.

The relatively unsatisfactory results of cardiac therapy are pointed out. The keystone of successful treatment is shown to be the control of the thyrotoxic state. The minimum of risk and the maximum of success are obtained by preoperative medical treatment, subtotal thyroidectomy at the most favorable stage, and postoperative medical treatment when necessary.

Craig, Henry R., and White, Paul D.: Etiology and Symptoms of Neuro-Circulatory Asthenia. Arch. Int. Med. **53**: 633, 1934.

To throw more light on certain aspects of neurocirculatory asthenia (in particular, its etiology and symptoms) the analysis of 100 cases is presented, 50 without and 50 with organic heart disease. In this series of 100 cases the females outnumbered the males, 69 to 31. The average age of civilian patients is higher than that among soldiers during the war, doubtless because one is dealing with all ages in the community. The ages in our series ranged from twelve to sixty-nine years, the average age for 100 patients being 35¾ years (31½ years for those with pure neurocirculatory asthenia and forty years for those with complicating organic heart disease). Only 9 per cent of the 100 patients were poorly developed or undernourished. The great majority were well developed and well nourished, or obese.

Neurocirculatory asthenia may be classified etiologically:

A. (1) That which follows severe infection, operation or other illness (9 per cent of the cases). (2) That following prolonged fatiguing work or heavy strain of some other sort without respite (10 per cent of the cases).

B. (1) That following a slight to moderate infection, operation or other illness (25 per cent of the cases). (2) That following a slight to moderate amount of fatiguing work or of strain of any sort (35 per cent of the cases).

C. That occurring after little or no strain, but tending to be much aggravated by illness or fatigue (20 per cent of the cases).

The borderline between the normal and the abnormal is ill defined, but it is best indicated by the appearance of symptoms in the course of the usual physical activities and excitements of daily life, which previously gave no symptoms, or which in the average person would produce no symptoms. Neurocirculatory asthenia is to be distinguished from "irritability of the heart" alone as shown by premature beats or paroxysmal tachycardia. It is also to be distinguished from neurosis as such, in which anxiety, hypochondriasis or hysteria is predominant. Twenty-five such cases were analyzed for comparison. It differs from ordinary neurasthenia, in which the flight into disease is manifested primarily by lack of energy, easy mental and physical exhaustion, and irritability. The authors have presented data with reference to symptoms in twenty-five cases of neurasthenia. "Neurocirculatory asthenia" is a term to be preferred to "effort syndrome" in designating the condition under discussion, since effort syndrome may be produced in normal people.

Palpitation, respiratory discomfort, precordial pains, or aches and exhaustion are the four cardinal symptoms of neurocirculatory asthenia. They occur in the order named with almost the same frequency (78 to 83 per cent of the 100 cases). Radiation of the precordial discomfort of neurocirculatory asthenia to the left arm, axilla, shoulder or scapula may occur (in 33 of 74 cases of this series). The more severe the precordial discomfort, the more likely the radiation. Sighing respiration and precordial tenderness are important confirmatory signs and are almost pathognomonic of neurocirculatory asthenia.

When neurocirculatory asthenia complicates organic heart disease, the symptoms are essentially the same in character and quantity as they are in the absence of organic heart disease. The fundamental mechanism of neurocirculatory asthenia remains obscure. Variations of the same mechanism in different persons, or indeed, even different mechanisms may give rise to the different combinations of symptoms and signs.

Reichert, Frederick Leet; Rytand, David A.; and Bruck, Edwin L.: Arteriosclerosis of the Lumbar Segmental Arteries Producing Ischemia of the Spinal Cord and Consequent Claudication of the Thighs. Am. J. M. Sc. **187**: 794, 1934.

The ordinary intermittent claudication in the arteriosclerotic is characterized by pain which is attributed to physiological processes developing in the working muscles easily fatigued due to impaired blood supply. It is associated with a lack of arterial pulsation in the feet and ankles, color alterations in the skin of the extremities on change of posture and roentgenographic evidence of calcification in the arteries of the legs.

Intermittent claudication because of weakness in the thighs and hips was the chief complaint of four nonsyphilitic arteriosclerotic patients who exhibited a spastic gait resembling that of a tabetic, who had no positive neurological signs and whose roentgenograms revealed calcification in the lower abdominal aorta.

The claudication of the thighs in these four patients was attributed to ischemia of the spinal cord produced by alterations in spinal branches of the arteriosclerotic lumbar segmental arteries arising from the abdominal aorta.

This hypothesis was strengthened by roentgenographic evidence of calcification in the terminal portion of the abdominal aorta and by experimentally produced claudication in the thighs of adult dogs after occlusion of the lumbar segmental arteries without interference with the blood supply to the thighs or remainder of the lower extremities, as shown roentgenographically by complete arterial injections of the animals.

Unilateral claudication developing after ipsolateral occlusion of one or more lumbar arteries in the dog afforded further proof that ischemia of the spinal cord was the cause of the claudication.

Krumbhaar, E. B.: Electrocardiographic Changes Accompanying Acutely Increased Pressure Following Pulmonary Artery Ligature. Am. J. M. Sc. 187: 792, 1934.

In an attempt to study the effect on the electrocardiogram of rapidly increased intraventricular pressures, records were taken before and after varying degrees of pressure were exerted on the pulmonary artery of anesthetized cats. The effect of increase in the pressure within the right ventricle as practiced in these experiments was regularly to increase the size of the P-wave in all Leads and frequently to produce extreme ventricular deflections like those seen in congenital heart disease. Sometimes signs similar to those of preponderance of the right ventricle appeared and disappeared when the clamp was loosed. When the clamp was about three-fourths closed, the right ventricle usually became much congested and dilated with a slow beat and the electrocardiogram sometimes showed a deep broad S_3, a high broad R_3, and in Lead II a deep A, medium R and no S. The possibility of such changes being due to bundle-branch block must of course be borne in mind. The T-wave, when not engulfed in the preceding S, sometimes became enlarged, sometimes inverted or diphasic, sometimes coming off near the point of R or S respectively, or at a new level from an overshoot of R (or S) or finishing at a new isoelectric period. Small extra waves, as if continuation of the T disturbance, were sometimes noted. It is suggested that changes in the ventricular complex, perhaps resembling those of right or left ventricular preponderance, especially if transient, may be due to changes in intraventricular pressure and not always to changes in muscle mass or position of the heart.

Buckbinder, William C., and Katz, Louis N.: The Electrocardiogram in Acute Experimental Distention of the Right Heart. Am. J. M. Sc. 187: 785, 1934.

The production of diffuse pulmonary emboli of metallic mercury following its introduction directly into the right heart or systemic venous circulation causes acute distention of the right heart. In the more chronic experiments a marked degree of right heart dilatation is regularly produced.

Instrumental compression of the pulmonary artery produces a marked ballooning out of the right side of the heart, followed soon after by a similar ballooning of the left side.

Acute distention or dilatation of the right heart in the above experiments is accompanied by no significant deviation of the electrical axis of the heart.

The peculiar aberrations of the ventricular complex (QRST) produced by mercury injection are illustrated, and evidence is presented to show that they arise because of short circuits set up by the intracardiac and extracardiac metal.

Edeiken, Joseph, and Wolferth, Charles C.: The Clinical Significance of Low T-Waves in the Electrocardiogram. Am. J. M. Sc. 187: 778, 1934.

A vertical or transverse position of the heart has a marked influence upon the ventricular waves of the electrocardiogram. In vertically placed hearts, R_1 is frequently low and often a low T_1 is associated. In transversely placed hearts T_3 is very frequently inverted and is sometimes associated with a low T_2; in many cases these findings are also associated with left axis deviation.

Although the association of low T_1 and R_1 is frequently encountered in vertical hearts, it is also found in the presence of cardiovascular damage, especially in rheumatic heart disease.

The association of a low T_1 and high R_1 is usually encountered in cases showing some cardiovascular abnormality, especially hypertension. It has, however, been observed in a few cases in which no cardiovascular abnormality was demonstrable.

The incidence of definite cardiovascular abnormality found in cases referred from wards and out-patient clinics for electrocardiographic study which could be classified in one or another of the electrocardiographic types under consideration was as follows: Type A (low T_1 and normal T_2) 83 per cent; Type B (low T_1 and T_2) 87 per cent; Type C (normal T_1, low or flat T_2 and inverted T_3) 63 per cent. In patients derived from the same sources but with normal electrocardiograms, the incidence of definite cardiovascular abnormality found was 41 per cent.

The percentages obtained for the incidence of myocardial damage or position of the heart as the cause of the low T-waves of the type classified under A and C depend mainly on the type of material being studied. In groups of presumably normal individuals, position is the more important; in groups suspected of heart disease, myocardial damage is the more important. In certain cases with heart disease, however, the T-wave changes may be due to altered position of the heart rather than to myocardial damage per se. The authors have obtained no evidence to indicate that small T-waves in all leads may be dependent on position of the heart.

Roentgen ray study of the heart is essential in attempting to evaluate the significance of low or flat T-waves in either Lead I or Lead II of the electrocardiogram.

For guidance in the clinical interpretation of electrocardiograms the authors believe the following statements are justified:

A. An electrocardiogram with a low R_1 and low T_1 and a normal T_2 points either to abnormality of the heart or to vertical position. When the heart is vertically placed, no significance can be ascribed to these findings as evidence of cardiac abnormality. When, however, the heart occupies its usual position, the low R_1 and T_1 suggest that it may be abnormal.

B. The association of a normal or high R_1 and a low T_1 offers strong but not certain evidence of cardiac abnormality.

C. The finding of small T-waves in all leads is probably rarely if ever dependent on position of the heart. It furnishes strong presumptive evidence of abnormality of the heart.

D. The combination of a normal T_1, a low or flat T_2 and an inverted T_3 may be due either to abnormality of the heart or to a more transverse position than is usual. When the heart is transversely placed, such an electrocardiogram may not be regarded as evidence of myocardial abnormality; when, however, the heart occupies the usual position, such a tracing suggests myocardial abnormality.

E. It is possible that in a small minority of cases, these various types of electrocardiograms may occur in the absence both of altered position of the heart and abnormality of the myocardium.

Book Review

THE SPAN OF LIFE AS INFLUENCED BY THE HEART, THE KIDNEYS AND THE BLOOD VESSELS. By Franklin R. Nuzum. Charles C. Thomas, 1933, 108 pages.

This well-made and attractive volume is designed to give information to the general public concerning varieties of cardiac disease, of Bright's disease, and of diseases of the arteries, their nature, their course, and their general management. It has become general knowledge that expectancy at birth has increased, and the reasons for the change in outlook have been attributed correctly to decrease in infant mortality and to decline in the prevalence of infectious diseases. What more natural, with these successes behind us, than to look for greater success still in the prevention and control of the "diseases" of later life? It is perhaps not ungracious to raise the question whether it is not premature to speak of certain aspects of several of these conditions as being either "diseases" or "degenerative," since there is no suitable classification of them into those which are natural processes incident to aging and those which may be regarded properly as disease or as pathological. To keep this possibility in view may save us in the sequel from serious disappointment. So far prevention, though desirable, and control have no significant successes, known to us, to their credit. How to discover them, itself awaits the development of a proper technic of analysis. But there is no reason why hope of amelioration of the state, so often unhappy, of old age should not be entertained; though the hope may be better tempered if it is bolstered by a knowledge of the facts.

In the pages of this little book there is collected an unusually large amount of knowledge without giving the impression of hurry or of undue compression. To one somewhat acquainted with its subject matter, the exposition seems lucid. But to those who have made similar attempts in brief compass to place at the disposal of laymen information on these matters, the chances of successful exposition are not too encouraging. It is the subject itself which must bear the major fault. Little is known, and much that is, is tentative; the mechanisms that are involved are just beginning to be studied and can scarcely be said to be understood. Yet there is no escape, in a society desirous of being instructed along each part of the way, from making the effort which has been made here. The amount of success which Dr. Nuzum has attained is great enough to encourage his successors to continue with the enterprise.

A. E. C.

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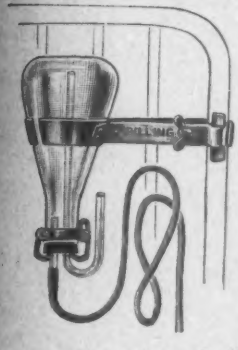

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